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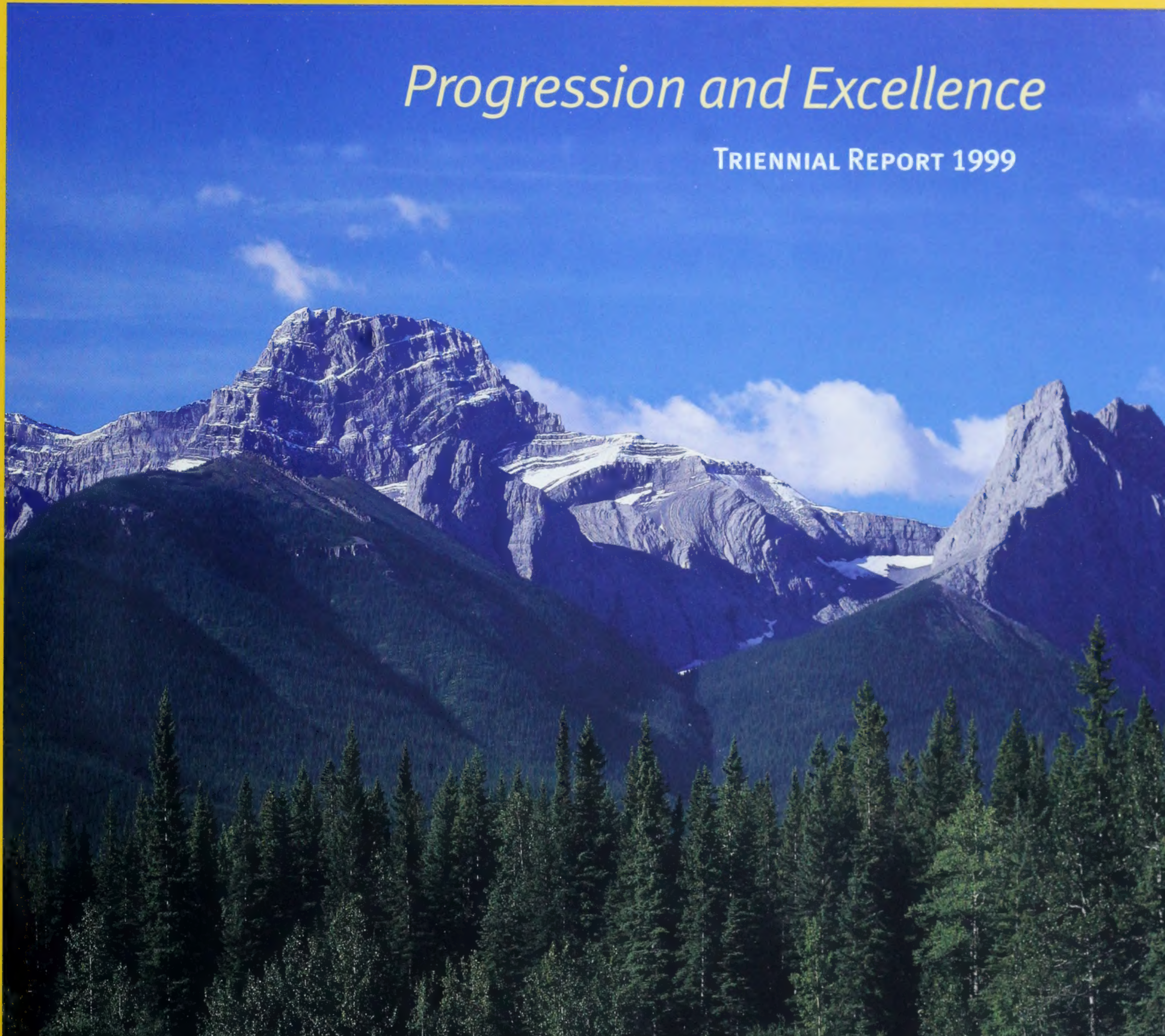
ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH



Progression and Excellence

TRIENNIAL REPORT 1999

Our Mission

We support a community of researchers who generate knowledge that improves the health and quality of life of Albertans and people throughout the world. Our long-term commitment is to fund basic, patient and health research based on international standards of excellence and carried out by new and established investigators and researchers in training.

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Note:
U of A refers to University of Alberta;
U of C refers to University of Calgary;
and U of L refers to University of Lethbridge throughout this publication.

Cover photo: Mountain view off 1A Highway west of Cochrane, Alberta

ALBERTA HERITAGE
FOUNDATION FOR
MEDICAL RESEARCH

Did you know?

Alberta is one of the top health research centres in North America? That's largely because of the Alberta Heritage Foundation for Medical Research.

The *AHFMR Newsletter* highlights the pioneering work of Alberta scientists, researchers, and innovators who are developing their health-care technology for the marketplace. It also includes valuable sources and practical information on health and medicine.

AHFMR also produces *Health Technology Assessment (HTA) News* for health professionals, which covers the most recent global assessments conducted on the efficiency and effectiveness of the technologies used in healthcare.

For information about AHFMR, please call Heritage Communications at 780/423-5727 or email postmaster@ahfmr.ab.ca. Check our website at: www.ahfmr.ab.ca

AHFMR Newsletter

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PROGRESSION AND EXCELLENCE

ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH

Triennial Report for 1996/97 to 1998/99

and Annual Report for 1998/99

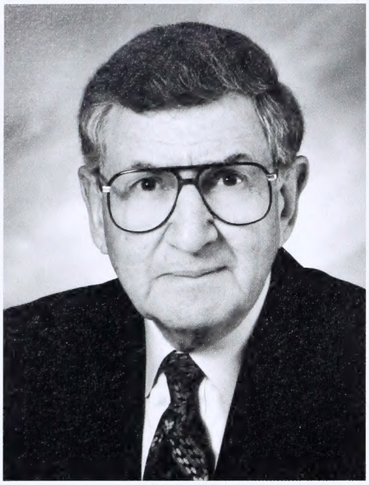
The AHFMR is a wonderful resource for Alberta whose programs have demonstrably benefited biomedical research in Alberta at the highest level. As such, it is not only something in which all Albertans should take great pride, it is also a national treasure. Long may it flourish.

– Dr. Michael Smith
Nobel Laureate and
International Board of Review Member

Introductory Section	2
Research Profiles	11
Medical Genetics	12
Cancer Research	18
Heart Research	26
Health Research	36
Cell Membrane Research	46
Immunology Research	54
Brain Research	60
Student Programs	68
AHFMR Program Information	75
AHFMR Consolidated Financial Statements	93
AFHR Financial Statements	107

On behalf of the Alberta Heritage Foundation for Medical Research's Board of Trustees, I am honoured to present the Triennial Report covering the years from 1996 to 1999.

As I look over the stories in the report that chronicle the past three years' worth of progress and success, I am struck by what a legacy AHFMR is for our province. The creation of the Foundation nearly two decades ago, informed by long-term vision and the funding of biomedical and health research by the highest standards of excellence, is ensuring now and far in the future, incalculable benefits for all Albertans. The presence and strength of AHFMR puts us ahead of most other jurisdictions of Canada. We in this province can rightfully boast of our provincial community of top-notch health researchers, of competitive and collaborative support for health research, and of the increasing number of discoveries, advances, and health technologies that are the direct results of AHFMR activities.



The long-term vision that informed the planning of AHFMR some 20 years ago continues to this day. This Report highlights an impressive array of activities, resulting from new programs and initiatives, and new heights of excellence that emphasize the Foundation's leadership role in health research provincially and beyond.

The growth in programs has been made possible by the parallel growth of the endowment. At March 31, 1999, the endowment from which grants and awards are made by AHFMR stood just below $1 billion. The endowment, and the more than $570 million invested in research excellence over the years, exemplifies the sound stewardship of the Board of Trustees and the responsible investment management of Alberta Treasury. It is a perpetual resource for excellence in biomedical and health research in our province for our children and their children.

"The endowment, and the more than $570 million invested in research excellence, exemplifies the sound stewardship of AHFMR's Board of Trustees and the responsible investment management of Alberta Treasury."

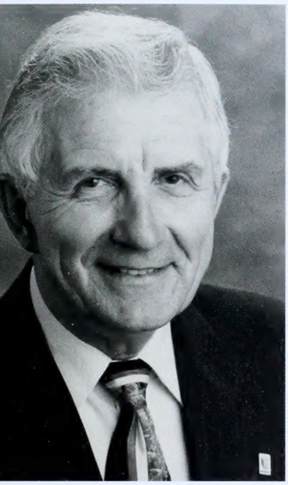
The responsibility that comes with directing the Foundation is not taken lightly by any AHFMR Trustee past or present. All the Trustees of AHFMR are successful in their chosen fields and they range from physicians and lawyers to businessmen, university presidents, and ranchers. All have contributed significantly to their communities through volunteerism and philanthropy. All consider their Trusteeship with AHFMR to be an important part of their careers. I thank them for their consistently sage advice and firm adherence to the AHFMR principle of first and foremost investing in people. On behalf of the Trustees, I applaud the brilliance and dedication of our extraordinary research community, and the exemplary leadership of Dr. Matt Spence and his talented and hard-working staff.

AHFMR researchers, on average, attract two to three dollars in outside funding for every Foundation dollar invested, and the estimated total puts health and biomedical research on the winning side of Alberta's ledger. The continued formula of sound, responsible financial stewardship, flexibility and responsiveness to the community's needs, innovative leadership in health research, and awards made by the highest standards of excellence, will stand AHFMR in good stead for decades to come.

Alvin G. Libin
Chairman

The progression of research is 99% of any scientist's life. Excellence during that progression is a given; it's hard to be mediocre and survive in a field where the expectations are so demanding for funding, publication, patents, and academic positions.

But how do we determine excellence? I'd like to think it's in the very nature of inquiry itself, the realizations that the right answers are ultimately the only things that fit, even if when they are found, it sometimes seems the discovery is more by luck than by logic!



It was the logical thinking and wisdom of AHFMR's originators who realized time and money had to be given to protect, nurture and develop the spirit of inquiry that lead to original discovery and scientific growth in Alberta. It is logic, not luck, that successive government leaders continue to share the vision of the independent nature of research and endorse wholeheartedly AHFMR's role in seeding the growth of what is now a brain trust to be reckoned with in the province. But beyond wise leadership, long-range vision, and carefully managed resources, the "secret" of AHFMR's success is simple: Excellence is the standard to which we aspire and excellence as judged by peer review is what AHFMR uses to guide its decisions about investing in health research in Alberta.

The 150 scientists and 450 scientists-in-training who currently receive AHFMR support exemplify this aspiration to excellence. Their achievements are connected in a continuum, from basic biomedical investigations to applied health technologies, to many of the medical and health advances you hear about in our province. It is these advances that are yielding new therapies and treatments to improve health, and new knowledge to train generations to come. It is the evolution of AHFMR to meet the new challenges that success brings that has led to the third successful review by an international committee of eminent scientists.

With this Triennial Report, spanning the years 1996-1999, we have described the dynamic research underway in eight broad areas of health and medicine. Profiled before each of these sections is a senior AHFMR scientist who exemplifies both progress and excellence. Most of these scientists have been funded from an early point in their careers by AHFMR (and by many other agencies). All have progressed *through* a system of excellence *to* heights of excellence. All have advanced their fields of research.

I invite you to turn the page and survey the successes at this nineteen-year mark in AHFMR's history.

Dr. Matthew Spence
President and CEO

"...it is believed that the structure to be developed may provide one of the finest, if not the finest, medical research plans on a pure research basis....that would exist in a country...."

Alberta Legislature, Fall 1977

Renewing our direction

Members of the International Board of Review (clockwise from top left): Dr. Michael Smith, Dr. David Goltzman, Dr. Karen Davis, Dr. Serge Carrière and Dr. Henry Dinsdale.

In October 1998, seven eminent scientists from around the world gathered in Edmonton to begin a five-day whirlwind tour of the province. Their objective was to meet as many people in the biomedical and health research community as possible to discuss with them the past six years of operations of the Alberta Heritage Foundation for Medical Research.

The seven members of the International Board of Review (IBR) had received briefing material and background information months prior to the visit. The IBR Chair, Dr. Henry Dinsdale, a well-known neuroscientist and a recent Order of Canada awardee, led the group through intense sessions in which they synthesized the information from the community with their own knowledge and experience to produce a review of performance and recommendations for future directions.

In December 1998, the Trustees of AHFMR released the report to the public with the help of Premier Klein. In it, the IBR endorsed the Foundation's growth over the past six years, its successes resulting from using international standards of excellence to support research, and the broadening of its portfolio to include new programs in health research support. Some of the recommendations advised

AHFMR supported researchers make world headlines:

April 1996: Dr. Leigh Field discovers a new gene that predisposes people to juvenile diabetes. One hundred thousand Canadians have juvenile diabetes.

December 1996: Dr. Michele Crites Battié and Dr. Tapio Videman report research findings that disc degeneration, one of the culprits in back pain, is due more to genetics than environmental causes. Ninety-five percent of all people suffer backpain at some point in their lives.

May 1996: Dr. Lung-Ji Chang announces clinical trials of drugs to treat brain and skin cancers.

1996: Dr. Sam Weiss discovers the existence of spinal cord stem cells, the "blueprints" to make nerve cells in the spinal cord.

November 1996: Dr. Karl Riabowol discovers a gene that stops cancer growth in laboratory experiments.

March 1997: Dr. Ron Zernicke and Dr. Peter Allen receive a grant, the first-ever of its type, from the Whitaker Foundation headquartered in the US.

fine-tuning existing AHFMR programs to enable faster and more direct response to the research community. Other recommendations called for more significant changes in programs and therefore operations, and were carefully considered.

AHFMR's Trustees discussed the recommendations with the Alberta community in a series of in-depth consultations with researchers held at the University of Lethbridge, the University of Calgary, and the University of Alberta. A meeting with other public stakeholders in the community was also held.

The consultation results helped inform the Trustees' decisions about many of the recommendations. Some were adopted immediately, while others were not acted upon right away because further monitoring and negotiations had to be undertaken. One recommendation for the cessation of the Technology Commercialization Program was not approved, in fact input from the community vividly demonstrated to the Trustees the necessity of not only keeping the program, but expanding it.

Convening an international board every six years to review its operations is part of AHFMR's legislated Act. The process is long and intense, requiring months of preparation by staff and IBR members. Like a report card, the IBR Report is an acknowledgement of strengths and an indicator of where strengths must be built to ensure continued success. But IBR recommendations and any Trustee decisions that are based on them only make sense in the context of community involvement. This is a process that AHFMR is committed to.

What lies ahead in the next six years? AHFMR will continue building stronger links to the community it serves. It will continue to examine its operations in light of its mission to ensure that success continues to build upon success. It will work with its stakeholders to enable the excellence of Alberta research to command attention on the national and international fronts. And it will continue to demonstrate to Albertans and people all over the world that the benefits of investment in research are not abstract. They are yielding cures, therapies, evidence and knowledge that help us all live better and healthier lives.

The $1.3 million grant will support a joint University of Calgary and University of Alberta graduate degree in bioengineering.

APRIL 1997: Dr. Marek Radomski finds a new way to prevent blood clots that cause heart attacks from forming. Heart disease is the leading killer of both men and women in North America.

OCTOBER 1997: Dr. Jonathan Schaeffer develops ground-breaking software to make DNA research easier with the support of AHFMR's Technology Commercialization Program.

OCTOBER 1997: Dr. Ted Tredget develops an innovative burn treatment with the help of AHFMR's Technology Commercialization Program. Infections from burns kill 90,000 North Americans yearly.

International Board of Review

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Professor Emeritus,
Department of Medicine
and Neurology
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Columbia

AHFMR responds to change

The past three years have seen a tremendous change in the biomedical and health funding landscape provincially and federally. AHFMR has responded to the changes with new initiatives, which capitalize on collaboration and enable Alberta researchers to compete on the national and international arenas.

The Health Technology Assessment unit housed at AHFMR is one of a number of similar groups around the world that are providing objective assessments on the tools used in health care. The HTA unit maintains working relationships with the Institute for Health Economics, the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) and other agencies in Canada and elsewhere. The Foundation is a member of the International Network of Agencies for Health Technology Assessment (INAHTA).

AHFMR's Opportunity Fund (AOF) created in 1997 offers matching funds for strategic research infrastructure initiatives proposed by institutions such as universities and regional health authorities. It is intended to match funds with the provincial government's Intellectual Infrastructure Partnership Program, and the federal government's Canadian Foundation for Innovation and the Canadian Health Services Research Foundation. As of March 31, 1999 the total amounts of moneys awarded through the AOF are $1.5 million.

Spring of 2000 is the official launch of the Canadian Institutes of Health Research, the new federal funding agency that will support research "from molecules to communities" as its mandate. The CIHR will absorb the Medical Research Council of Canada and its estimated annual budget will be $500 million. Dr. Matthew Spence, President and CEO of AHFMR and a member of the Interim Governing Council of CIHR comments, "Opportunities for AHFMR researchers for federal support are now better than ever. The CIHR's mandate to support collaborative initiatives within a health research continuum dovetails with AHFMR's strengths and programs."

NOVEMBER 1997: Dr. John Remmers, the inventor of CPAP, the standard treatment for sleep apnea around the world, develops a refined version of the device, with AHFMR's Technology Commercialization support.

NOVEMBER 1997: Isotechnika, an Edmonton based biotechnology company, develops a breath test for ulcers. Isotechnika was started with the help of AHFMR's Technology Commercialization support. Ulcers affect 60% of the population.

FEBRUARY 1998: Drs. Carol Adair and Reg Sauve show that second-hand smoke doubles the risk for ear infection in children during the first three years of life. Middle ear infections in children cost the Canadian Health system $500 million annually.

FEBRUARY 1998: Kelly James develops a prosthetic leg that enables wearers to have a normal gait . His innovation was assisted with funds from AHFMR's Technology Commercialization Program.

MARCH 1998: Dr. Frank Witkowski and Dr. Wayne Giles develop an imaging system that captures heart attacks in progress. Heart disease costs the health system $19 billion annually.

MAY 1998: Dr. Sam Lee and Dr. Mark Swain conduct clinical trials of new therapies to help Hepatitis B and C patients. Three hundred thousand Canadians have Hepatitis C.

JULY 1998: Dr. David Hodgins develops a self-help book for problem gamblers. Nearly 5% of the population has a severe gambling problem.

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University of Washington
Seattle, WA

Dr. Anita B. Roberts
National Cancer Institute
Bethesda, MD

Dr. Gary L. Stiles
Duke University
Durham, NC

NOVEMBER 1998: Dr. Patrick Lee discovers that the reovirus, a harmless cold virus present in all humans, can kill cancer.

DECEMBER 1998: Health Canada approves Dr. Lorne Tyrrell's discovery of an effective drug to treat Hepatitis B. 250,000 Canadians suffer from Hepatitis B.

FEBRUARY 1999: Dr. Alastair Buchan develops a new safety technique to treat stroke patients with clot-busting drugs. Three people die daily in Alberta from stroke.

MAY 1999: Dr. Raj Rangayyan develops new breast screening technology. There were 1500 cases of breast cancer in Alberta and the Northwest Territories in 1999.

MAY 1999: Dr. Ji-Won Yoon discovers a juvenile diabetes trigger. Juvenile diabetes affects 13,000 Albertans.

MAY 1999: Dr. Charles Holmes finds high levels of a toxin implicated in liver cancer in some blue green algae food supplements.

The world applauds

Dr. Peter Allen (Biomedical Engineering) &
Dr. Ron Zernicke (Kinesiology)
Recipients of a Whitaker Foundation Award for the development of a provincial Biomedical Engineering Graduate Program.

Dr. Stephen Archer (Cardiology)
1999 NATO Collaborative Grant (North Atlantic Treaty Organization)

Dr. Chris Bleackley (Biochemistry)
Named Distinguished Scientist by the Medical Research Council of Canada, and an International Research Scholar by Howard Hughes Medical Institute, 1997

Dr. Andrew Braun
(Pharmacology & Therapeutics)
Recipient of the Third Molson Young Investigator Award

Dr. K.C. Carrière (Mathematics)
1996-2000 National Health Research Scholar Award from Health Canada (National)

1994-1997 Manitoba Health Research Scholar Award (Provincial)

Dr. Carol Cass (Oncology)
1999 YWCA of Edmonton Women of Distinction Award in Health and Medicine (Award patron: AHFMR)

Dr. Michele Crites Battié & Dr. Tapio Videman
(Rehabilitation Medicine)
Volvo Award in Clinical Sciences by the International Society for the Study of the Lumbar Spine

Dr. Cam Donaldson (Community Health Sciences and Economics)
The Svare Chair in Health Economics

Dr. Neil Duncan & four colleagues
(Biomedical Engineering)
Volvo Award in 1998 for the best research paper in spine biomechanics research

Dr. John Elliott (Medical Microbiology & Immunology)
Co-recipient of a 1999 Juvenile Diabetes Foundation/Medical Research Council Diabetes Research Network Partnerships Award

Dr. Gordon Francis (Medicine)
1998 Canadian Lipoprotein Conference / Bristol-Myers Squibb new investigator award

Dr. Robert French
(Physiology & Molecular Biology)
Medical Research Council of Canada Distinguished Scientist Award

Dr. William Ghali (Medicine)
Petro-Canada Young Innovator Award

Dr. William Ghali & Dr. Paul Mains
(Biochemistry & Molecular Biology)
The Watanabe Distinguished Achievement Award for overall excellence

Dr. William Ghali & Dr. Patrick Lee
The Cochrane Distinguished Achievement Award for excellence in research

Dr. Patrick Lee (Microbiology & Infectious Diseases)
City of Calgary Signature Award for outstanding contributions made by Calgarians

Dr. Dennis Hall (Chemistry)
1998 Bio-Mega / Boehringer Ingelheim Thesis Award (National)

1998 Research Innovation Award from Research Corporation (International)

Dr. Alan F. Kingstone (Psychiatry)
1996 Young Psychologist Award from International Congress of Psychology (International)

Dr. Paul Kubes (Physiology & Biophysics)
Faculty of Medicine Distinguished Achievement Award in Research

Dr. Richard Lehner (Pediatrics)
Canada Research Award for Basic Lipoprotein Science

Dr. Jonathan Lytton
(Biochemistry & Molecular Biology)
1996/97 recipient of the Calgary Herald Young Innovator Award

Karen Madsen (Medicine)
University of Alberta Medical Students' Association annual teacher of the year award, Phase I

Jeffrey Man (MD student)
First place in the biochemistry/ molecular biology category of the 40TH annual National Student Research Forum, U.S. (Work funded by an AHFMR summer studentship)

Dr. Miguel Martin-Carabello (doctoral student)
Neuroscience Canada Foundation Award

Dr. John McKenna (Post-doctoral fellow)
Neuroscience Canada Foundation Award

Dr. Marek Michalak (Biochemistry)
First winner of the Astra / Pharma and CFBS competition in Molecular Biology

Leonie Moorhouse Herx (doctoral student)
Neuroscience Canada Foundation Award

Dr. Janice Morse (Nursing)
1997 Baxter Foundation Episteme Award for excellence in nursing research. Baxter award given by the Sigma Theta Tau International Honor Society of Nursing.

Glen Newell (doctoral student)
Neuroscience Canada Foundation Award

Dr. Kamala Patel (Immunology)
1997/98 recipient of the Calgary Herald Young Innovator Award

Dr. Barry Phipps (Biological Sciences)
1996-97 recipient of the Molson Young Investigator Award

Dr. Quentin Pittman (Neuroscience)
Neuroscience Canada Foundation Award

Dr. Arthur Prochazka (Neuroscience)
Neuroscience Canada Foundation Award

Dr. Alexander Rabinovitch (Medicine)
Co-recipient of a 1999 Juvenile Diabetes Foundation/ Medical Research Council Diabetes Research Network Partnerships Award

Dr. Karl Riabowol
(Biochemistry & Molecular Biology)
The Cochrane Distinguished Achievement Award for excellence in research

Faculty of Medicine Distinguished Achievement Award in Education and Research

Dr. Robert Ryan (Biochemistry)
Named a Medical Research Council of Canada senior scientist

Dr. Paul Schnetkamp
(Biochemistry & Molecular Biology)
Faculty of Medicine Distinguished Achievement Award in Research

Dr. Richard Schulz (Pediatrics)
Merck Frosst Award in Pharmacology

Dr. Keith Sharkey
(Physiology & Biophysics)
1999 Young Investigator Award from the Canadian Association of Gastroenterology

Dr. Gaynor Spencer (Post-doctoral fellow)
Neuroscience Canada Foundation Award

Dr. Michael Surette
(Microbiology & Infectious Diseases)
1998 Young Investigator Award from Bio-Mega Boehringer Ingelheim Canada

Pamela Valentine (doctoral student)
Neuroscience Canada Foundation Award

Dr. Dennis Vance (Biochemistry)
Elected a Fellow of the Royal Society of Canada

Dr. John Wallace
(Pharmacology & Therapeutics)
1999 Distinguished Research Award of the Gastrointestinal Section of the American Physiological Society

Medical Research Council of Canada Senior Scientist Award

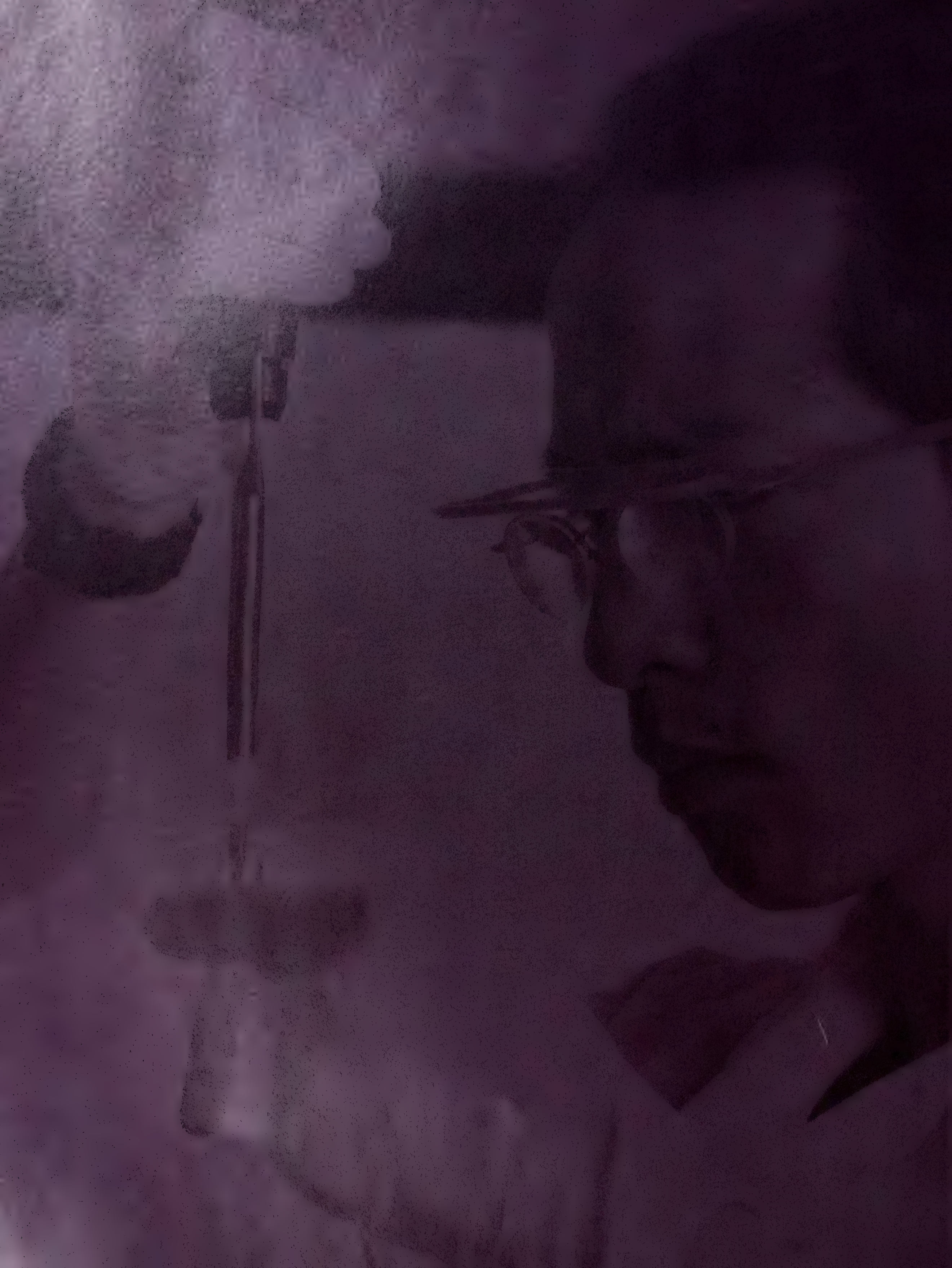
MRC Michael Smith Award for Excellence

Dr. Brent Winston (Medicine)
The Canadian Society of Clinical Investigation, Joe Doupe Award as the Young Clinical Scientist of the Year

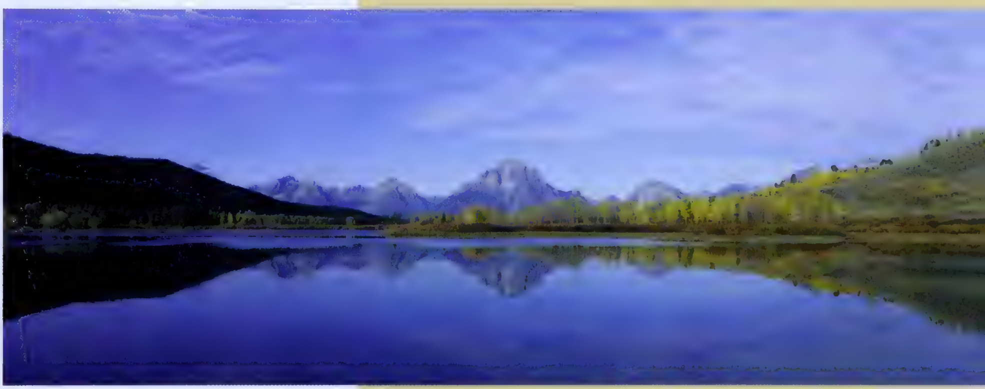
Dr. Richard Woodman (Medicine)
The McLeod Distinguished Achievement Award for excellence in teaching

1998 recipient of the Watanabe Distinguished Achievement Award for overall excellence

Dr. Ji-Won Yoon
(Microbiology & Infectious Diseases)
Sixth Korean Broadcasting system Award in Scientific achievement for his outstanding accomplishments in diabetes research



MAKING PROGRESS: ACHIEVING EXCELLENCE



Through its contribution to career opportunities, economic growth and the stature of Canadian research over the years, the Alberta Heritage Foundation for Medical Research has galvanized government support for health research. The world-class scientific research it has fostered within the province of Alberta has enriched the entire Canadian research community and remains a source of pride both nationally and internationally.

– Dr. Henry Friesen
President
The Medical Research Council of Canada

Exploring new horizons

These days, if she's not in the lab, you might find Dr. Leigh Field somewhere in the sky over Calgary.

The Heritage Scientist has been busy logging the necessary flight time to get her private pilot's licence. "It has to do with exploration," she says of why she likes to fly. "It's really nice to be up in the air where you have to focus all of your attention on the immediate task of keeping this piece of equipment running. At the same time, you get to discover the beautiful vistas of the earth below."

> *"At the time we began our research very few people thought it was worth doing; that's the whole idea behind exploration–looking for something and not knowing whether you'll find it."*

This love of exploration also propels her research. "If your driving motivation as a scientist is that you find research fun and exciting, then that keeps you going," Dr. Field says.

In the past six years, the Heritage Medical Scientist and University of Calgary medical geneticist has identified three genes related to juvenile-onset (Type 1) diabetes—a remarkable accomplishment when a short time ago even the existence of these genes was thought to be unlikely. "When we began our research, very few people thought it was worth doing," Dr. Field reflects. "That's the whole idea behind exploration—looking for something and not knowing whether you'll find it."

She now has a fourth gene for diabetes locked in her sights. Ironically, it was born out of research that she began over 15 years ago on a gene determining antibody structure. Back then, researchers thought it was improbable that antibody genes could influence susceptibility to diabetes. "Some people would jokingly say, 'Oh, you're the person who believes that!' when they would find out what I was doing," the researcher chuckles. Now she thinks she has convincing evidence for a fourth gene. Her groundbreaking work has helped raise the level of knowledge for the genetic basis of the disease sky-high.

Her three major research areas all involve identifying genes predisposing to common but genetically-complex disorders: insulin-dependent (type I) diabetes mellitus, cleft lip with or without cleft palate, and dyslexia.

She notes that, just as in flying a plane, it takes many people working together to keep her research aloft. "It's impossible to function, in genetic research, without collaboration," Dr. Field says. "I have extensive collaborations with other scientists throughout the world." These include a dyslexia research collaboration with Calgary Heritage-supported researcher Dr. Bonnie Kaplan; teaming up with other scientists in Canada and Denmark on diabetes research; and establishing collaborations in the United States, India, Turkey, and China to collect information for research on the genetics of cleft lip and palate, a common birth defect. "It is only in my early diabetes studies that I could say I was working by myself. And even that isn't true, because I was collaborating with clinicians to get blood samples," she notes. "I couldn't do any of these projects by myself. Collaborations are absolutely critical."

Dr. Leigh Field
Heritage Medical Scientist at the University of Calgary
Supported by AHFMR for 14 years

Dr. Field attributes much of her success to the support from AHFMR and other funding agencies that allowed her to pursue curiosity-driven research. “So many important discoveries happen by accident,” she notes. “But making discoveries takes many, many long hours of work. Often, much of that work doesn’t lead to anything that seems to be significant. That’s the nature of basic research.”

Looking into the future, Dr. Field says the ultimate goal of her research is to draw a complete picture of how different genes interact to produce the predisposition to the diseases she studies. “None of the investigations in complex diseases has reached an understanding yet of how different genes work together. The future of genetics is going to be understanding interaction between genes,” she predicts. “That’s a completely different order of magnitude than isolating single genes that appear to have effects, but without an understanding of how they exert those effects.” It may seem a lofty goal, but the continued hard work, determination, and tenacity of researchers such as Dr. Field could make it a down-to-earth reality.

Recent Achievements in Medical Genetics

- Insights into the genetics of glaucoma, cleft lip/palate, dyslexia, and herpes simplex virus
- Establishment of new Department of Medical Genetics at the U of A
- Development of a major improvement on a technique that makes it easier for scientists to detect DNA
- Determining why DNA polymerases make a particular error known as “simple repeats” when replicating DNA. An error in DNA replication can cause human diseases, such as cancer.
- New information about genes

Genetics Resources

University of Alberta, Department of Medical Genetics
http://www.medgen.med.ualberta.ca

Human Gene Map
http://www.ncbi.nlm.nih.gov/SCIENCE96/

Human Genome Project Information
http://www.ornl.gov/TechResources/Human_Genome/home.html

Diabetes Resources

Alberta Foundation for Diabetes Research
http://www.afdr.ab.ca

The Diabetes Research Foundation
http://www.jdfc.ca

Canadian Diabetes Association
http://www.diabetes.ca

Biomedical Engineering

University of Alberta,
Department of Biomedical Engineering
http://www.bme.med.ualberta.ca

(Clockwise from top left): Drs. Jonathan Lakey, Garth Warnock, Chris Bleackley, James Shapiro, Allan Murray, Norm Kneteman, Greg Korbutt, John Elliott, Alex Rabinovitch, and Ray Rajotte.

Stemming the surge of diabetes

Diabetes affects 1.5 million Canadians, including children and young adults. It is the leading cause of blindness and kidney failure, and contributes to stroke and other serious medical complications. The World Health Organization projects the growing incidence of diabetes to reach epidemic proportions in the 21st century.

Basic research by Heritage-supported scientists at both the University of Alberta and University of Calgary has resulted in significant advances in our knowledge about this chronic disease, its treatment and possible prevention. Given the strength of diabetes research in Alberta, a cure for the disease seems more likely than ever.

University of Alberta researchers Dr. Ray Rajotte, Dr. Garth Warnock, and Dr. Norm Kneteman were the first in Canada to successfully transplant islet cells in order to treat diabetics without insulin injections. Their goal of achieving insulin-free diabetes moved closer to reality in 1999, when a team led by Dr. Alexander Rabinovitch, Dr. John Elliott, and Dr. Rajotte received a $2.7 million national grant to continue work in this area. Other team members were Drs. Chris Bleackley, Greg Korbutt, Jonathan Lakey, Eddie Ryan, James Shapiro, and Drs. Warnock and Kneteman. The scientists were one of two teams to receive awards given out in 1999 by the Juvenile Diabetes Foundation and the Medical Research Council of Canada.

Dr. Leigh Field has discovered three genes for juvenile-onset diabetes, and is pursuing a fourth. Dr. Jin-Won Yoon made headlines in spring 1999 with his discovery of new information on what triggers a common form of juvenile-onset diabetes and a possible way to prevent it. Dr. Yoon and his research team discovered that a protein in the pancreas is key to the appearance of the disease in mice. They also found that immunizing young mice prone to the disease could help prevent its onset.

Researchers mentioned:

At the University of Alberta:

Dr. Alexander Rabinovitch and Dr. Chris Bleackley are AHFMR Medical Scientists.

Dr. Garth Warnock and Dr. John Elliott are AHFMR Senior Scholars.

Dr. Greg Korbutt is an AHFMR Scholar.

Dr. Ray Rajotte, Dr. Norm Kneteman, and Dr. Eddie Ryan are AHFMR alumni.

Dr. Jonathan Lakey is an AHFMR Post-doctoral alumnus.

At the University of Calgary:

Dr. Leigh Field and Dr. Jin-Won Yoon are AHFMR Medical Scientists.

Improving diabetic health

More than half of diabetics suffer from diabetic neuropathy, a disorder that progressively destroys the nerves. Dr. Doug Zochodne is interested in finding out what causes the different types of diabetic nerve damage so they can be prevented or reversed. Dr. Zochodne is currently testing new drugs that may promote growth in nerve cells.

Better education for diabetics

Dr. Philip Hardin, a diabetes specialist, is researching diabetes education methods that could lead to shorter, more intense information sessions specifically for newly diagnosed patients. The seven-hour education module he is evaluating covers physiology, diet, blood monitoring, and potential complications.

From research to diagnosis

Dr. Diane Cox came to the University of Alberta in 1996 to help build the new Department of Medical Genetics, which was set up thanks, in part, to a $1 million AHFMR Independent Establishment Grant. The Department, which houses AHFMR researchers Dr. Moira Glerum, Dr. Michael Walter, Dr. Susan Andrew, and Dr. Rachel Wevrick, is considered unique in combining clinical, diagnostic, and basic research facilities in one unit.

(Left to right): Dr. Moira Glerum, Dr. Diane Cox, and Dr. Rachel Wevrick

Sights ahead

When Dr. Bill Pearce came to Edmonton more than two decades ago to head up the new Ocular Genetics Clinic, he began to track families with rare eye diseases. He didn't have today's sophisticated molecular genetics technology, so he used blood markers. Dr. Pearce had an inkling his family database would have a use in the future, and he is thrilled that not only is it one of the most substantive databases of its kind in existence, but that top-notch scientists are recruited to the University of Alberta because of the opportunity to work with it.

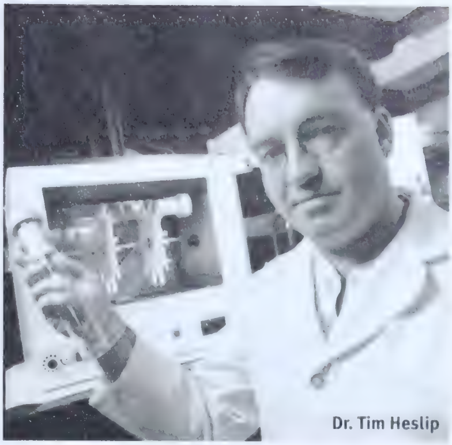
Dr. Michael Walter is one of those scientists. When he found that much of the database started by Dr. Pearce chronicled diseases of the front part of the eye, he initiated several projects that may someday yield valuable tools to fight a leading cause of blindness—glaucoma. Dr. Walter heads an international research group that is close to identifying the genetic causes of glaucoma.

Early detection of blindness

When Dragan Krstic's daughter began experiencing eye problems, he turned to his neighbour, ophthalmologist and medical researcher Dr. Ian MacDonald, for testing. Dr. MacDonald found that

Mr. Krstic had choroideremia, an incurable condition that leads to blindness. His daughter's vision problems were unrelated, but her test results identified her as a carrier, who will not, because of the genetics of choroideremia, develop the disease herself. Dr. MacDonald, a world authority on choroideremia, developed the diagnostic test used on the Krstics, a technology that has attracted international attention. His ongoing research also contributes valuable information to the Alberta family database of rare eye diseases.

Dr. Ian MacDonald with his neighbour Mr. Dragan Krstic


Dr. Tim Heslip

Lessons from the fruit fly

Molecular biologist Dr. Tim Heslip is using what he has learned about the genetic material of the *Drosophila* fruit fly to identify similar genes involved in the progression of arthritis and joint injury in humans. In particular, he is interested in how the fly uses the genetic means of growing a limb to repair joint injury. The ultimate goal of his research is to develop techniques of molecular biology such as gene therapy to treat arthritis and joint injury.

From unseen to three-dimensional

Dr. Brian Sykes successfully brought together key players to fund the University of Alberta's new National High Field Nuclear Resonance (NMR) Centre, also known as NANUC. AHFMR's contribution to the 800-megahertz NMR was $700,000 of the approximately $3 million contributed by provincial and national funding partners. NANUC is the only facility of its kind in western Canada.

NANUC's technology makes it possible for scientists working in fields as diverse as the pulp and paper industry and cancer research to see the three-dimensional configuration and interaction of molecules.

Researchers mentioned:

Dr. Rachel Wevrick, Dr. Moira Glerum, Dr. Susan Andrew, and Dr. Michael Walter are AHFMR Scholars at the U of A.

Dr. Brian Sykes is an AHFMR Medical Scientist at the U of A.

Dr. Tim Heslip is an AHFMR Scholar at the U of C.

Dr. Douglas Zochodne is a Heritage Scholar at the U of C.

Dr. Philip Hardin, an Edmonton-based physician, received support from the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness.

Dr. Bill Pearce is the former Head of the Ocular Genetics Department at the U of A.

Dr. Ian MacDonald is Chair of the Department of Ophthalmology at the U of A. He received support through the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness.

Reovirus: cancer fighter

His discovery that a particular virus, called the reovirus, may be effective against certain forms of cancer made international headlines in late 1998.

Since then, Heritage-supported researcher Dr. Patrick Lee has given countless interviews to reporters anxious to tell the world about what they have dubbed "cancer's magic bullet." When asked about his newly acquired celebrity status, Dr. Lee shifts uneasily in his chair. Being a media star is an uncomfortable role for someone who spends most of his time in his lab and in his modest University of Calgary office.

He acknowledges that recent public attention has helped bolster support for his research, but it has also resulted in another unforeseen consequence. Since the discovery was announced, Dr. Lee has personally answered innumerable heart-wrenching telephone calls from desperately ill cancer patients who want to help test his "cure." Unfortunately, he must gently, but firmly, tell them he can't help them. Although some added attention can be expected from a discovery of such promise, there's a big difference between potential and reality in basic scientific research, Dr. Lee emphasizes. "I don't want to get people's hopes too high. We have yet to prove that the reovirus will work against cancer in humans."

A virus is like a parasite because, in order to survive and grow, it must first attach itself to a cell and then find a way to enter it. When a virus emerges from a targeted cell, it will have replicated itself thousand fold. Dr. Lee has discovered that the reovirus can replicate only in cells with a highly active biochemical pathway called the Ras signalling pathway. It's an important finding, because an active Ras signalling pathway is found in many cancer cells.

The reovirus appears to be very effective against 80% of cancers, including pancreatic, prostate, and breast cancer, as well as brain tumours. Tests on mice with implanted human brain and breast cancer tumours have dramatically demonstrated this potential. Dr. Lee has shown that injecting live reovirus into these tumours results in the virus replicating and killing the cancer cells.

The next step in the research is to apply these findings in a small, carefully conducted human clinical trial. Phase I testing is expected to begin shortly in Calgary, with support from the AHFMR's Technology Commercialization Program.

> *"There's a big difference between potential and reality in basic scientific research."*

Dr. Lee first learned of the reovirus during post-doctoral fellowship training in the late 1970s. He studied under Duke University researcher Dr. Bill Joklik, known as a founding father of modern virology. "In those days, we were not looking for a cure for cancer," Dr. Lee notes, alluding to the importance of curiosity-driven research. "You never know where a breakthrough will come from." The reovirus find is the result of nearly 20 years of meticulous work.

Dr. Lee brought his new knowledge back to Canada in 1981. Originally from Hong Kong, he moved to Edmonton in the 1960s, obtaining a bachelor of science and a doctorate in biochemistry from the University of Alberta. The chance to return to Alberta, obtain Heritage funding, and be involved in the University of Calgary's new medical school drew him back to the province. "Those were really, really exciting times. There were a number of young

Dr. Patrick Lee

Technology Commercialization Program grant recipient at the University of Calgary

Supported by AHFMR programs for 10 years scientists conducting dynamic research. And everybody was gung-ho about the establishment of the Alberta Heritage Foundation for Medical Research," recalls Dr. Lee.

Nearly two decades later, his enthusiasm is still evident. Dr. Lee fosters an excitement for research in the researchers-in-training who pass through his lab and he believes absolutely in the importance of investing in young scientists. "If you don't have the people power, you have nothing when it comes to research," Dr. Lee suggests.

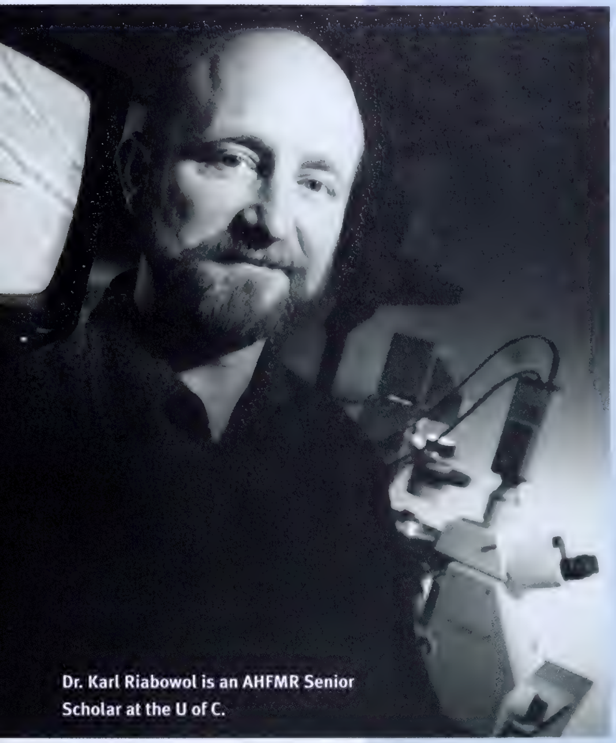
At the moment, Dr. Lee has 11 students working with him. So far he has graduated 11 Ph.D. and six M.Sc. students who have gone on to careers in industry, academia and science. He also collaborates with researchers in Calgary, Edmonton, and other parts of the world.

"The most exciting thing about science is you wake up in the morning and say to yourself, 'Gee, what I am going to find out today?'" he says with a note of wonder in his voice. "I can still remember the day we found out that the reovirus could have a cancer connection. It was the most exciting day of my life."

Recent Achievements in Cancer Research

- Development of state-of-the-art computer technology to aid in the identification of breast cancer tumors
- Discovery of a gene, ING-1, that inhibits the growth of tumors in several types of cancer
- New clues about the way the immune system recognizes cancer cells
- Discovery of a "magic bullet" virus, reovirus, that is proving effective in mice against 80% of cancers
- Evidence that aberrant activity of the human c-Src gene is key in the development and progression of breast cancer
- Development of new 3-D x-ray technology that reduces patients' exposure to harmful levels of radiation
- Attacking cancer in the body using a gene gun to fire pellets loaded with genetic material directly inside tumor cells
- Development of a research and intervention program designed for women with gynecological cancer
- Development of an exercise program to study the role of physical activity during and following cancer treatment
- Identifying the need for comprehensive cervical cancer screening in Alberta

Learning cancer's progression



Dr. Karl Riabowol is an AHFMR Senior Scholar at the U of C.

Ongoing research on a gene discovered in 1996 by Dr. Karl Riabowol and his post-doctoral fellow, Igor Garketsev, is showing that the gene, ING-1, may be key to preventing the growth of more than one type of cancer cell.

Dr. Riabowol and his team have been working to understand how the gene functions in normal cells and how it shuts itself off in cancer cells. This information could help researchers selectively activate ING-1 in tumour cells to stop them from multiplying. If this can be done, the gene could, in the near future, become an important new treatment for cancers of the breast and brain.

How ING-1 works appears to be related to the way cells age and undergo "programmed" cell death (PCD). As aging progresses, normal cell division and growth slow. In cancer, however; cell division and growth dramatically accelerate. Dr. Riabowol is trying to determine what cellular mechanisms are in place to limit normal cell growth, in the hope that he can use those same mechanisms on cancer cells.

His biggest challenge will be to make sure that ING-1 and other tumour suppressors target cancer cells, not normal cells. If he can decipher ING-1 regulation in cells, Dr. Riabowol might be able to devise a way to turn up the gene. Cancer cells would then be affected, and normal cells would enter temporary senescence, the end of cell division, until the gene could safely be lowered to regular levels.

Testing to extend life

Nearly 20 years ago, cancer researcher Dr. Linda Pilarski began a collaboration with Dr. Andrew Belch that resulted in a fresh look at the cells in multiple myeloma, a fatal cancer of the bone marrow. They noted the presence of many highly abnormal B cells in the blood of people with this disease. They determined that these abnormal cells were related to the cancer. This discovery has recently led to a new way of monitoring myeloma. Although it has no known cure, there are ways to treat the disease that help patients live better and longer. With assistance from the AHFMR's Technology Commercialization Program, Dr. Pilarski has developed a novel test kit to monitor malignant cancer cells in patients with myeloma. The test is a relatively non-invasive way to gauge the success of therapy on a regular basis.

Increasing precision in mammograms

Because the breast is mostly made up of soft tissue, visual differences between developing tumors and normal tissue can be slight. Computer engineer Dr. Raj Rangayyan is developing state-of-the-art computer scanning to sharpen mammogram images and increase the contrast between regular tissue and cancerous growth. By using mathematical processes, the researcher, whose work is supported through the Health Research Fund, can also map out the shape and boundaries of tumours. This technique is intended to help radiologists determine whether a tumour is cancerous or not, and how far it has spread.

Helping people live with cancer

A growing consciousness that people need to live with cancer, not in spite of it, is leading to innovative research to develop treatments that help patients in all aspects of their lives, not just the physical. Dr. Kerry Courneya is conducting one such research project. In collaboration with cancer epidemiologist Dr. Christine Friedenreich of the Alberta Cancer Board in Calgary, he looked into the role of exercise in the lives of cancer patients. They found that very few studies exist on the subject, which led to Dr. Courneya's current investigations into the role of exercise in improving the quality of life for patients both during and following cancer treatment. Dr. Courneya is working with the Cross Cancer Institute's Dr. Tony Fields to recruit cancer patient volunteers.

Dr. Raj Rangayyan

Cancer and female sexuality

The broad spectrum of cancer treatment programs in Alberta demonstrates that improving quality of life for cancer patients is just as important as curing them of the disease. Dr. John Robinson, a clinical psychologist, developed a unique research and intervention program designed for women who have gynecological cancer. Dr. Robinson is a specialist in addressing and treating patients' concerns about the effects of cancer and its treatment on their sexuality and sexual functioning.

Tracking alternative therapy use

Preliminary results from a research project by Dr. Suzanne Tough and Dr. Heather Bryant of the Alberta Cancer Board, suggest that nearly 50% of colon cancer patients follow alternative therapies such as yoga, acupuncture, and aromatherapy throughout the course of their illness.

Dr. Tough is seeking to answer questions about this largely unexplored area, including how alternative and conventional therapies are combined, why people use them, and the types of alternative therapies they engage in.

The two-year, Alberta-based study of nearly 1,000 patients is run jointly by the Alberta Cancer Board and the University of Calgary.

Cells at war

Dr. Hanne Ostergaard's work is focused on how killer cells, or cytotoxic T-cell lymphocytes, know what to kill and what to spare. Her answers in the area of cell signalling may contribute to the growing store of knowledge scientists are compiling about our body's ability to resist or succumb to disease.

Dr. Ostergaard is mainly interested in how killer cells seek out an abnormal cell. "I am not interested in the killing mechanism *per se*," she says. "I want to find out how the T-cell crawls around in tissues, and what happens when it comes in contact with an antigen—a tumour cell or a virally infected cell. There are a number of molecular interactions that must occur before the tumour cell or virally infected cell can be eliminated."

Dr. Hanne Ostergaard

Minimizing radiation risk

Frequent x-rays used to track scoliosis may expose patients to dangerous levels of radiation that could put them at risk for leukemia. Ph.D. student Steve Boyd is one of several U of C researchers involved in a collaborative project overseen by Kinesiology Dean Dr. Ron Zernicke, that use harmless three-dimensional laser scans instead of x-rays to test the torsos of afflicted patients. The laser scans also yield clearer pictures that give doctors a better idea of the progression of the disease.

Dr. Don Fujita

Learning the secrets of Src

Dr. Don Fujita has spent more than 15 years teasing out the secrets of the c-Src protein and the c-Src gene that makes it. Src and the nine or so other protein members of the Src family are required for the growth and development of various types of normal cells. When somehow mutated or abnormal, they are capable of causing cancer.

His lab, in collaboration with Dr. H. J. Kung of the United States, was the first to clone the human cellular Src gene. "We were fairly certain that its Src protein played a role in some human cancers. Sure enough, it is involved in human colon and breast cancers.

"Now we are in the process of finding what mechanisms make Src normal and which ones make it abnormal leading to cancers." says Dr. Fujita.

Researchers mentioned:

Dr. Linda Pilarski and Dr. Andrew Belch are based at the U of A and receive support from AHFMR's Technology Commercialization Program for their Multiple Myeloma test.

Dr. Raj Rangayyan is based at the U of C and receives support through the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness.

Dr. Kerry Courneya is based at the U of A and holds an AHFMR Independent Establishment Grant and receives support through the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness.

Dr. John Robinson is based at the Tom Baker Cancer Centre and receives support through the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness.

Dr. Hanne Ostergaard is an AHFMR Senior Scholar at the U of A.

Dr. Don Fujita is an AHFMR Medical Scientist at the U of C.

Dr. Heather Bryant, with the Alberta Cancer Board, and Dr. Suzanne Tough, based at the U of C, receive support through the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness.

Steve Boyd is an AHFMR student at the U of C.

Dr. Ron Zernicke is the Dean of Kinesiology at the U of C and is an AHFMR alumnus.

Cancer Resources

Canadian Cancer Society
Toll-free: 1-800-661-2262

http://www.cancer.ca/indexe.htm

Canadian Cancer Society Alberta/NWT
http://www.cancer.ab.ca

Alberta Cancer Board
http://www.cancerboard.ab.ca

Alberta Program for the Early Detection of Breast Cancer
Toll free: 1-800-667-0604

Canadian Breast Cancer Foundation
http://www.cbcf.org

Canadian Ophthalmological Society
http://www.eyesite.ca/index-english.htm

Following the beat to excellence

How did the fly-fishing son of a Yukon bush pilot, who wanted nothing more than to own his own helicopter fleet, become a top scientist?

Heritage Medical Scientist Gary Lopaschuk "blames" it on two things. The first was having a father who was adamant his son must have the university education the father never had. The second was a defining moment that ended his life as a pharmacist and began his scientific career. He was working at a drugstore one day when a customer inquired about having a year-old prescription filled. When he asked her what the prescription was for, he was told it was none of his business. "I realized I wanted it to be my business, but not in the way the customer meant. I wanted my contributions to result in better health for people—new knowledge perhaps leading to better medicines. I wanted to do it in a way that was meaningful for me."

The world of research beckoned. Further study at the University of British Columbia culminated in a doctorate in the area of calcium transporters, key molecules involved in energy metabolism, the conversion of food into fuel. Dr. Lopaschuk first focused his studies on diabetes, a disease where energy (sugar) is not used properly.

The heart, Dr. Lopaschuk knew, was the optimal energy consumption model to study because hard-working heart muscle needs fuel for every heartbeat. He opted for further study in the lab of Dr. James Neely in Pennsylvania. Dr. Neely was the first scientist in the world to develop a way to measure a whole heart using energy, a critical advancement because study of a single heart cell does not give a true picture of heart function. Single heart cells are metabolically inactive. It takes many of them working together to make the heart contract.

Despite the superb mentorship of Dr. Neely, Dr. Lopaschuk and his wife knew they didn't want to stay in the United States. By that time, they had a young family, and quality of life was a big issue. He was recruited to Toronto's Hospital for Sick Kids and then brought to the West with AHFMR support.

"My wife and I had a five-year plan," he says, "We really wanted to live in Vancouver, so we gave Edmonton five years. Well, I've been approached twice in the past decade by Vancouver institutions and each time we said no. Edmonton grows on you, it's home now."

The quality and extent of heart research in Edmonton, in part led by Dr. Lopaschuk, has also grown. He is now Head of the University of Alberta's Cardiovascular Research Group, an impressive team of cardiologists and basic scientists, many of them Heritage-funded, who together and singularly make headlines. Dr. Lopaschuk's work is among the most newsworthy.

For years, researchers thought that when the heart was in the throes of ischemia (obstructed blood flow), it wasn't able to use its primary fuel source: fatty acids. Using tech-

"I wanted my contributions to result in better health for people—new knowledge perhaps leading to better medicines. I wanted to do it in a way that was meaningful for me."

Dr. Gary Lopaschuk
Heritage Medical Scientist (as of July 1, 1999)
at the University of Alberta
Supported by AHFMR for 12 years

niques refined from his work with Dr. Neely, Dr. Lopaschuk was the first to show that, in actuality, traumatized heart cells produce an excess of fatty acid. Because the already damaged heart tissue does not have the oxygen required to use the complex fatty acids, it becomes further damaged.

Dr. Lopaschuk's investigations led to his serendipitous use of two older diabetes drugs that, in the lab, showed remarkable success in getting damaged hearts to use glucose (sugar) instead of fat. Glucose, requiring less oxygen than fatty acids, is much easier for traumatized heart tissue to use, resulting in much less damage. He subsequently founded a company, Metabolic Modulators Research Limited (MMRL), with the help of AHFMR's Technology Commercialization Program, to modify key enzymes by drugs for potential development into new heart therapies.

He's also found three enzymes that directly control how the heart uses fatty acids. This discovery has led to collaborations with Heritage researchers at the University of Alberta and the University of Calgary, and with scientists throughout Canada, the United States, and Europe. He also leads a Medical Research Council of Canada (MRC) group at the University of Alberta that is composed of Heritage researchers Drs. Rick Schulz and Ivan Rebeyka, and colleague Dr. Sandy Clanachan.

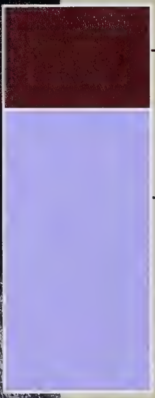
Dr. Lopaschuk sees the future challenge for the research world is in recruiting young people into the field. Important mentorships throughout his career helped him succeed. In turn, he has mentored scores of students and post-doctoral fellows, who are now living all over the world, and working at universities and in industry.

The pressures of running a research lab, competing for funding, and starting up a company don't faze him. He uses an analogy drawn from his experiences during his university years as a fly-fishing guide in the far North: "Fly-fishing is all about fooling the fish," he says with a grin. "Research gives the same satisfaction. You never know where it will go, but what you do and where you go depends on self-motivation. It's very exciting to design experiments even if one in ten works. And like letting the fish go, you can always change direction."

AHFMR investment from 1996-99 nearly quadrupled by the Basic Heart Function Group at the U of C

Five of the six scientists in this group were recruited to the U of C with AHFMR funding. They have now been funded for a total of 73 person-years.

Twenty-four research trainees who have worked in five of these scientists' labs have been AHFMR-funded for a total of $560,000



$1,900,000	total amount awarded by AHFMR to the six scientists*
$5,500,000	total external funding attracted by group
$7,400,000	total funding of group

*Figures are approximations and are rounded off to the nearest thousand.

Heart researchers (back row): Drs. Jonathan Lytton, Paul Schnetkamp, Wayne Giles, Paul Kubes; (sitting): Drs. Robert French and Robert Clark

Deciphering the signals of heartbeats

Ah, the mysteries of the heart! Poets have wrung beauty from the agonies and ecstasies it causes on a metaphysical level. On the purely physical level, the main function of this fist-size, four-chambered, electrically powered pump is to push blood around our bodies. But for many scientists, including Dr. Wayne Giles, this is where the true mysteries of the heart lie: in the signals that govern its life-giving beat.

Dr. Giles is a major contributor to the understanding of electrical impulses that cause the heart to beat spontaneously. His work in the areas of pacemaker activity and irregular heartbeats has yielded valuable information for the design of pacemakers and defibrillators—devices that jolt the heart with electricity to stop erratic beating. His research has also helped in the development of drugs to control dangerous heart rhythms that, if uncorrected, can lead to heart attacks.

Dr. Giles heads a crack research team at the University of Calgary, funded by the Medical Research Council of Canada and known as the Ion Channel and Transporter Group, which is delving into the basics of heart and blood vessel function, as well as vision. Four of the scientists, Drs. Jonathan Lytton, Paul Schnetkamp, Paul Kubes and Robert French are Heritage researchers. Colleague Dr. Robert Clark completes the team. The Group's research will help further understanding of the structure and function of the key ion channels that function like gatekeepers, allowing substances, for example the calcium needed for each heartbeat, in and out of heart cells. Many diseases of the heart are caused by ion channel malfunction.

Dr. Giles and Heritage scientist Dr. Frank Witkowski have developed unique high-resolution movies that show what happens when a heart attack triggers ventricular fibrillation, a deadly heartbeat irregularity. This technology may lead to improved heart defibrillators. Dr. Giles and Dr. Witkowski are part of an international research team.

Researchers mentioned:

Dr. Robert French and Dr. Paul Schnetkamp are AHFMR Medical Scientists at the U of C.

Dr. Frank Witkowski is an AHFMR Medical Scientist at the U of A.

Dr. Wayne Giles is AHFMR alumnus and is the Head of the Department of Physiology and Biophysics in the Faculty of Medicine at the U of C.

Dr. Paul Kubes is an AHFMR Senior Scholar at the U of C.

Dr. Jonathan Lytton is an AHFMR Scholar at the U of C.

Correcting a fundamental flaw

Dr. Katherine Kavanagh

Irregular heart rhythms are not uncommon; and most, originating in the top chambers of the heart, are harmless. It's when the heart's lower two chambers, called ventricles, experience faulty rhythm, that lives are threatened. Often ventricular fibrillation arises after a heart attack, and if untreated, can lead to further heart attacks. Cardiologist Dr. Katherine Kavanagh is mapping the electrical signals that heart cells use to communicate and keep the heart beating. She is contrasting these signalling patterns to how cells communicate during ventricular fibrillation, when signals are interrupted. If she can identify pathways of signalling that can be manipulated, the information could be used in developing new therapies to correct faulty heart rhythm.

Bringing a good idea to market

Dr. Gary Lopaschuk's research on compounds that could reduce tissue damage during heart attacks attracted a lot of attention from pharmaceutical companies in the United States and Japan. Even before he finished setting up his company, Metabolic Modulators Research Ltd., it had an industrial partner (Chugai Biopharmaceuticals, Inc.) and had signed a long-term deal for the development of techniques based on one enzyme. However, Dr. Lopaschuk knew there were several other enzymes to target and wanted to keep the rights to develop them further.

It was clear that if MMRL was to do this, the company would need extra resources and advice, as well as expertise in medicinal chemistry. Resources and advice have come from the Technology Commercialization Program of AHFMR, and other supporting agencies. The expertise comes from University of Alberta chemistry professor Dr. John Vederas, who has a collaborative agreement with MMRL.

While research continues, the focus on the business side is developing marketing and business plans. And Dr. Lopaschuk wants to take his in-house development to the point of getting Investigational New Drug approvals. "I think development beyond that would be impractical for us," he says.

"The advantage of doing this independently is that we will get higher royalties and attract more interest from companies. It's the difference between a concept and a group of potentially viable compounds."

At the moment, MMRL has four or five target enzymes to explore. And because the main thrust of Dr. Lopaschuk's research is to understand the mechanics of these heart enzymes, new targets will likely be found. The company will use this research to maintain its lead position.

"I think we have a three-year window to develop new compounds," he says. "It's only a matter of time before the big pharmaceutical companies duplicate our drug development process. What we've done with Metabolic Modulators Research is to create a way for us to capitalize on our lead and get more value out of the research here in Alberta. Without MMRL, we'd be selling our technology at an early stage out of the province, and most likely out of the country."

Dr. Ivan Rebeyka

Home-grown expertise

Over the past year, AHFMR's Technology Commercialization Program has seen a doubling of applicants for its three phases of funding. TC awards support a company's journey on the sometimes rocky road from discovery to a viable healthcare tool or therapy. That growth is echoed in the emerging need for people who not only understand research, but have the business background to translate innovation into commercial success.

To help develop expertise in the province, AHFMR established a TC Internship Program in 1996. The one-year program places research graduates with an industry partner. Interns develop their expertise in areas such as intellectual property development, writing clinical investigation plans, and establishing Good Laboratory Practices and Good Manufacturing Practices. So far, 13 interns have received support from AHFMR with placements resulting in the University of Calgary's University Technologies International, the University of Alberta's Industry Liaison Office, and with private companies.

Correcting faulty hearts

Dr. Ivan Rebeyka heads the only program in Alberta that surgically treats children, and some adults, born with congenital heart defects. Yet Dr. Rebeyka conserves time from his hectic schedule to conduct research. His research is devoted to finding new and better ways to improve outcomes for heart patients. One of his projects is focused on finding safer ways to stop and restart infants' heart during surgery.

Dr. Rebeyka believes that the earlier heart problems can be treated, the more developmental damage can be averted. He is exploring the possibility of conducting heart surgery while fetuses are in the womb. "What can start out as a very minor problem in the womb in the early stages of development, can grow into a major defect by the time of birth. I want to see the day when we can correct heart defects before a child is born," Dr. Rebeyka says.

Dr. Todd Anderson

From hormones to heart health

Hormone replacement therapy (HRT) can offer relief from the symptoms of menopause, but the decision to take it is not always easily made. For a minority of women who have a breast cancer gene, HRT increases the risk for the disease. However, three facts also influence their decision: heart disease is the number one killer of women; risk for it increases in post-menopausal women; and the hormone estrogen protects against it. Scientists attribute about half of estrogen's protective action to its effect on cholesterol levels. Cardiologist Dr. Todd Anderson is investigating what the other half of the hormone's role is in lowering the risk of heart disease.

Dr. Anderson's ongoing research focuses on the function of the endothelium, a layer of tissue about the thickness of plastic sandwich wrap, that lines all blood vessels in the body. He suspects that the hormone estrogen, through its effects on certain molecules, may help keep the endothelium elastic, which is vital for keeping blood vessels free of fatty deposits and ultimately lowering the risk of atherosclerosis. He is conducting long-term clinical trials to compare the effects of estrogen in hormone replacement therapy with a regime that lowers cholesterol to the same degree, in order to gauge what effect estrogen has on blood vessel health. What he learns may guide physicians and women in making decisions about taking hormone replacement therapy.

Giving vulnerable hearts a fighting chance

One of the biggest risks for frail or elderly patients recovering from major surgery, disease, or injury is infection. Sepsis, the umbrella term for the spread of infection throughout the body, is one of the biggest killers in North American intensive care units.

When sepsis rages through a patient's body, it triggers profound changes in all cells, including the cells of the heart, which then produce massive amounts of a substance called nitric oxide in an effort to stave off the infection. But excess amounts of nitric oxide not only kill off pathogens, they also damage heart cells.

"The heart is trying to fight back, even if it gets damaged by the very weapon it is using to save itself," comments Dr. Rick Schulz. His research on the interplay between nitric oxide and heart function is yielding exciting new knowledge on how to prevent injury to heart cells during serious health crises.

Dr. Rick Schulz

Assessing heart treatments

When aspirin's powers were shown by research to extend far beyond pain and fever control and into the realm of being a first-line defence against heart disease and possibly colon cancer, it's no wonder that physicians and patients wanted to learn more. AHFMR's Health Technology Assessment Unit (HTA) was there to help. The Unit, moved to AHFMR from Alberta Health and Wellness in 1995, takes requests for assessments on health technologies—the tools, therapies, and devices used in health care—from government, healthcare professionals, and institutions. HTA staff analyze available global literature and prepare a written assessment which is available to the public.

A 1998 HTA assessment concluded that aspirin was indeed effective for certain people at high risk for heart attack. For those who have a low risk, aspirin prophylaxis may be injurious, since aspirin can have side effects including gastrointestinal problems. Not enough information was available to show aspirin's role as a primary weapon in preventing colon cancer, although evidence pointed to a reduction in the disease with long-term use of the drug.

AHFMR's HTA Unit is unique in the province but has counterparts all over the world. The vital task of providing objective, unbiased information on which to base healthcare and delivery decisions is not an easy one. Recently, an assessment of a group of drugs for lowering blood cholesterol by a Canadian HTA office led to the office being sued by a pharmaceutical that manufactured one of the drugs. The subsequent court case, which was lost by the pharmaceutical company, put pressure on the HTA office and raised issues of censorship. The case was discussed in an article, co-authored by Dr. David Hailey, then Director of AHFMR's HTA unit, in the prestigious journal, *Science*.

Researchers mentioned:

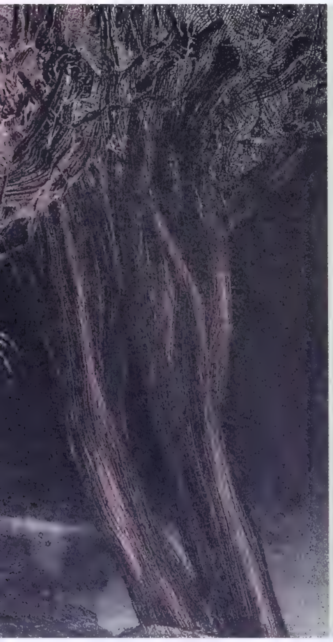
Dr. Katherine Kavanagh is an AHFMR Scholar.

Dr. Todd Anderson is an AHFMR Clinical Investigator.

Dr. Richard Schulz is an AHFMR Senior Scholar.

Dr. Ivan Rebeyka holds an AHFMR Independent Establishment Grant.

Dr. Heather Fraser holds an AHFMR Post-doctoral fellowship.



Lipid-Cholesterol Resources

High Cholesterol Levels and CHD
http://adminweb.ucis.dal.ca/cprrc/cholest.htm

Elevated Cholesterol Information and Resources
http://www.pslgroup.com/ELEVCHOL.HTM

Heart Resources

The Alberta Heart Health Program
780/427-2653

Heart and Stroke Foundation of Canada
http://www.hsf.ca/main_e.htm

Climbing the ladder to excellence

The fear of having a heart attack is common in North America, and rightly so. According to the Heart and Stroke foundation of Alberta, cardiovascular disease—disease of the heart and blood vessels—is responsible for 40% of all adult deaths in Canada and the United States.

This is where recent University of Alberta Ph.D. graduate Dr. Heather Fraser wants to make a difference. The Alberta-born pharmacologist accepted an AHFMR-supported post-doctoral fellowship at the prestigious Johns Hopkins University in Baltimore. There, she has joined a team of heart experts in the lab of Dr. Eduardo Marban.

"Most of the twenty post-docs in Dr. Marban's lab are not North American," Dr. Fraser says, "You get to learn how research and science are done in other countries, and all kinds of ways of thinking." Although she admits that moving to the famous Johns Hopkins was "a little intimidating at first", Dr. Fraser has landed in an atmosphere of support and stimulation that will allow her research in the next two years to flourish.

With one research project, she is looking at solitary ailing heart cells and how certain drugs improve their contractions. With another, she will work on describing the molecular mechanisms that go awry inside the muscle cells of injured hearts.

Dr. Fraser is confident she will succeed under Dr. Marban's guidance. "Good mentors don't come knocking on your door," she explains. "You have to go looking for them." Mentoring plays a key role in Heather Fraser's life. When she's not in the lab on the receiving end, she is in the community providing guidance and encouragement to children. In Edmonton, she volunteered with a program designed to let young women explore the idea of a career in science. Now in Baltimore, Dr. Fraser reads books with inner city children and teaches elementary students basic science and nature experiments.

One of her top supporters has been her Ph.D. supervisor, University of Alberta pharmacologist Dr. Sandy Clanachan. Dr. Fraser looks back with gratitude to Dr. Clanachan's role in advancing her skills. Because of him, she says, "I've reached the point in my career where I have ideas of my own and see them followed through. It's like a rite of passage when you no longer have to do just what you're told."

The next step for the 30-year old pharmacologist will be the crucial transition from post-doctoral fellow to independent professional life. "I think that the Marban lab gives her a very good pedigree for coming back to Canada in an academic position," says Dr. Clanachan. And of all the opportunities available to post-doctoral fellows, returning to a university lab of her own in western Canada to continue her research in heart disease remains Dr. Heather Fraser's number one vision of success.

Basic research can save lives

Like many of us, Dr. Charles Holmes is probably happiest outdoors on a warm summer day.

But there the similarities stop, as Dr. Holmes spends a good amount of time near pungent pockets of lake algae. For algae, in particular the blue-green algae that "blooms" in the heat of summer, is the focal point of his groundbreaking biomedical research—basic research that may well be saving lives.

A dozen years ago, Dr. Holmes had completed a master's degree in biochemistry at the University of Calgary as one of the very first Heritage-supported students, and then a doctorate with renowned hormone specialist Dr. Phil Cohen in Britain. He was working as a post-doctoral fellow at Montreal's branch of the National Research Council, focusing on how crucial proteins called phosphatases enable the body to carry out a number of vital functions, with different results in different tissues. For example: in heart cells, they help the heart beat; in liver cells, they help break down carbohydrates for energy.

"I realized that this kind of toxin crisis was only going to increase, and that there was a real niche for Canadian expertise in this area."

He was also pondering his future, wondering if he should do another post-doctoral stint or strike out on an independent research path. Then the Prince Edward Island toxic shellfish crisis struck. The public panicked, and the government and the scientific community scrambled to contain the damage and provide answers for the phenomenon. In the chaos surrounding the crisis, Dr. Holmes saw a career path that quite remarkably linked the basic research that he loved with direct human-health application.

"My research into protein phosphatases led me right to marine toxins, because that's the chief thing some of these toxins target in organisms. They shut down this fundamental metabolic activity—that's why they are so lethal. The P.E.I. crisis woke us all up. I realized that this kind of toxin crisis was only going to increase, and that there was a real niche for Canadian expertise in this area."

He was recruited to the University of Alberta in the early 1990s with Heritage funding and continued his investigations into the molecular action of marine toxins on crucial proteins. The Heritage Senior Scholar has lots of raw material to work with—the simple plant form algae has been in existence since the beginning of time and is found worldwide. The rapid growth of blue-green algae, usually during the hottest part of summer, is called a bloom. Normally, blooms are annoying because they clog the shoreline of lakes and release a bad odour. However, in some blooms, periodically, the algae release toxins called microcystins.

Scientists are noticing an increase of algae blooms, attributed to the increased use of fertilizers in farming. The chemicals in agricultural runoff provide ideal food for algae to bloom more frequently and more extensively. Frequent blooms increase the possibility for microcystins in water supplies, although most drinking water filtration systems in the country meet Canadian minimum standards for purity.

Even if microcystins are consumed in water, the standard thinking is that the digestive system destroys these toxins. The real danger lies in the use of contaminated water for such medical procedures as kidney dialysis,

Dr. Charles Holmes (and research technician, Mireille Estaphan)

Heritage Senior Scholar at the
University of Alberta

Supported by AHFMR for 18 years

where many litres of water pass directly into a patient's bloodstream. In Canada, strict safety standards make dialysis one of the safest medical procedures. In other countries, however, when standards were not rigorously monitored, the results have been lethal.

One exciting result of Dr. Holmes' work has been the development of a kit that shows, with a colour change, the presence of microcystins in a matter of hours. He anticipates a world market for the kit, because it is easy to make and easy to use. In China, for example, it is estimated that 60% of the drinking water is contaminated with microcystins. Currently he is contracted by a major Canadian city to check the drinking water sources regularly for toxins.

His work also indicates that the long-held belief that toxins are destroyed by the digestive process may not be accurate. Blue-green algae has long been ingested as a food supplement and when people take it they often report higher energy levels. But, says Dr. Holmes, this could be due to the presence of microcystins.

"The boost of energy some people get when they eat blue-green algae results from a reaction in the liver. Microcystins change how the liver breaks down glycogen, a complex carbohydrate we use for fuel. The result is similar to a rush of adrenalin. However, because microcystins are linked to liver cancer, we can't be sure the digestive system destroys all the toxins."

The worrisome part of this scenario is that "health food" is not subject to government inspection. So if periodic blooms of algae have contaminated a source for algae food supplements, the consumer has no way of knowing. In early 1999, Dr. Holmes was checking various brands of blue-green algae food supplements to see if microcystins were present. He was shocked to find that many of them were not only contaminated, but with levels far exceeding the Canadian maximum. When he sent these results to Health Canada, federal scientists replicated his findings and acknowledged his tests to be the most sensitive in the world. Health Canada issued a nationwide health advisory urging Canadians to use caution, and especially not to feed blue-green algae to children, until further research has been conducted.

Dr. Holmes' lab was contracted by the government to further test algae supplements. As often happens in research, the unexpected leads to new gains. "Health Canada sent us the supplements in an organic solvent. Our test was not designed to use with solvent, but we proceeded anyway. To our surprise, we found the solvent increased the sensitivity of detection. We've now been able to introduce this new fivefold sensitivity in our kit."

In spite of the publicity his findings generated, Dr. Holmes maintains a scientific skepticism. "We may well find out that tiny amounts of microcystins are beneficial to people, much as other poisons in minute quantities are, if not good for you, then at least not harmful."

Dr. Holmes leads the field by maintaining one of the top academic laboratories in Canada for detecting and working with algae toxins. He also maintains important collaborations with colleagues at the University of Alberta and at the University of British Columbia.

Basic biomedical research rarely has immediate human-health application; instead, it yields vital chunks of information—pieces of the puzzle that increase our overall knowledge in increments. At a time when basic research is beginning to be recognized as a blue-chip investment for government and industry, those working in the field can feel some relief. Dr. Holmes' research, however, is a rare and powerful example of basic research with an immediate global impact.

Dr. Colin Macarthur with a young cyclist

Making the world safer for children

More children die from unintentional injury than from all other causes combined. If we close the gap between what we know about injuries and what we do about them, many could be prevented.

Dr. Colin Macarthur involved in research on the prevention of childhood injury. Specifically, Dr. Macarthur aims to identify the major types of childhood injury in Alberta, apply prevention programs based on the evidence, then evaluate the programs.

Dr. Macarthur supervises several students in the Community Health Sciences Department at the University of Calgary who are working on injury-prevention research projects. One student, Karin Dymond, is the 1998 AHFMR Lionel E. McLeod Health Research Scholarship winner, and is taking the combined MD/MSc joint-degree program. Her research is focused on the cost-effectiveness of different strategies to increase helmet use by children.

Dr. Macarthur is also on the advisory body of the Alberta Centre for Injury Control and Research, a provincial organization based at the U of A and headed by Dr. Louis Francescutti. An ardent crusader in the effort to bring more recognition and research dollars to the field of injury prevention, Dr. Francescutti has also developed innovative technology to help rescue workers respond to emergency situations. His RAMPART-EMS computer program lets emergency response staff treat and track injuries at the scene of the emergency and is being tested in Strathcona County. ROAM-I.T., the company founded to develop the software, is supported through AHFMR's Technology Commercialization Program.

Researchers mentioned:

Dr. Colin Macarthur is an AHFMR Population Health Investigator at the U of C.

Dr. Louis Francescutti's company, ROAM-I.T., is based in Edmonton and partially supported through AHFMR's Technology Commercialization Program.

Healthy communities

Culture, tradition, and community dynamics play an enormous role in health delivery and education. Dr. Nancy Gibson, a medical anthropologist and Chair of the Human Ecology Department at the University of Alberta, observed first-hand non-Western approaches to healing some 20 years ago when she was a nurse in Sierra Leone. She is drawing on that experience to guide research that may help selected communities in Alberta. Dr. Gibson and her research team of healthcare professionals and community partners, are trying to discover what stops people from completing the tuberculosis treatment in Aboriginal and immigrant populations, where the disease has the highest incidence in the province. In their study, they'll also be observing strategies these communities use to cope with disease. Her hope is to develop different and better treatment programs that will ensure better health in vulnerable communities.

Learning more about women's health

▶ Twenty Blackfoot women from the Blood and Peigan reserves in Southwestern Alberta are using storytelling, an important component of Aboriginal culture, to share how they healed from addiction and dependency. Drs. Virginia McGowan and Russel Barsh are listening to the stories to understand what has helped the women change. The researchers will be contrasting the experiences of these women, who have been in trouble with the law and who have struggled with substance abuse, with those of Aboriginal women, including women in southeastern Australia. The insights gained from this research will be considered by Blackfoot comunity members to inform policy and program development in their communities.

Dr. Lynn Meadows

▶ Does your gender, the colour of your skin, or the amount of money you make affect your health? Dr. Lynn Meadows thinks so. She is conducting a three-year study of mid-life women's health that will take into account their social, cultural, and economic circumstances. Components of the study look at Aboriginal women's health perceptions and those of the elderly. The field of women's health is under-researched, and initiatives like the federal government's new requirement to include women in clinical trials for new drugs are a positive step in remedying the situation. Dr. Meadows' study is the first of its kind in Alberta and will identify women's major health concerns so that recommendations can be made for practical interventions.

Dr. Tapio Videman and Dr. Michele Crites Battié

A new look at the causes of back pain

Back pain caused by disc degeneration afflicts people all over the world, regardless of race, culture, economics or social standing. Billions of dollars are spent on therapies and treatments to alleviate suffering. Long thought to be the result of physical stress on the spine from vibration or activity, research conducted by Dr. Tapio Videman and Dr. Michele Crites Battié has shown that the true source of back pain lies for the most part in our genes. Their findings could indicate very different ways to treat back pain in the future.

Preventing falls in the elderly

▶ Geriatrician Dr. David Hogan is looking into the reasons why fall prevention isn't as well managed as it should be. Nearly one third of seniors fall at least once a year, resulting in injury, curtailed independence and costly medical care. Dr. Hogan and research team have designed a research project that is also an intervention to see if falls can be prevented by identifying risk factors and dealing with them. Rather than suggest radical changes to an older person's life, the team works with the person's physician and existing support services to integrate non-disruptive changes that will have the greatest impact on reducing falls.

▶ Three participants in AHFMR's SEARCH program tackled research projects in their communities aimed at preventing falls in the elderly. Two of the projects targeted healthy seniors living on their own and concluded that for these people, intervention programs work best. The third project, focused on frail seniors living in nursing homes showed strategies to build up strength, such as physiotherapy, worked best. The results of the SEARCH projects have been used to develop a "falls prevention" program, which includes a strength-building component, in the Mistahia Health Region.

Dr. Jean Wessel and Sharla King

New directions to reduce pain

▶ Physiotherapist Dr. Jean Wessel, Dr. Yagesh Bhambhani, and doctoral student Sharla King are looking at the effects of an education program, an exercise program, and a combination program of education and exercise on volunteers who have fibromyalgia, an unexplained pain syndrome. Pinpointing strategies that work to reduce pain may offer insights into what causes the condition.

▶ Back problems will plague most people on earth at some point in their lives. Biomedical engineer Dr. Neil Duncan is studying the discs found between the bones of the spine to understand how they break down over time and why this problem is more severe in certain people. He's examining the mechanical and biological properties of the disc tissue to see what induces change in the cells. His research may contribute to the growing field of tissue bioengineering, where human tissue is artificially grown to be implanted into the site of injury.

Researchers mentioned:

Karin Dymond is the 1998 Lionel E. McLeod Health Scholarship winner at the U of C.

Dr. David Hodges is based at the U of C and receives support through the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness.

Dr. Virginia McGowan is based at the U of L and receives support through the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness.

Dr. Lynn Meadows is an AHFMR Population Health Investigator at the U of C who also receives support through the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness.

Dr. Nancy Gibson is based at the U of A and holds an AHFMR Independent Establishment Grant.

Dr. Jean Wessel, Dr. Yagesh Bhambhani, and Sharla King are based at the U of A and receive support through the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness.

Dr. Neil Duncan is based at the U of C and holds an AHFMR Independent Establishment Grant.

Dr. Michele Crites Battié is based at the U of A and holds an AHFMR Independent Establishment Grant.

Dr. Tapio Videman is an AHFMR Health Senior Scholar at the U of A.

Physician and SEARCH II participant, Dr. Ron Gorsche

A team approach

Dr. Ron Gorsche has had a few unique patient encounters as a rural physician in the southern farming community of High River, Alberta. "A farm wife once drove up on my lawn with her tractor. It was my day off, but she knew where I lived and wanted to talk to me about the meals her father was getting at the hospital," he says, adding that patients have also sought him out in the barber's chair and the grocery store check-out. While the town's seven doctors take turns being on call, in a small community it seems there is nowhere for off-duty physicians to hide. "My partner had somebody crawl up onto his roof, where he was making some repairs, because the guy wanted a prescription. So he wrote one for him on a shingle. The pharmacist didn't bat an eye, just filled it," Dr. Gorsche notes wryly.

Underlying the humor in these anecdotes is the prevalent issue faced by rural and urban doctors alike—the often-stressful burden of being on call, available to patients 24-hours a day. Dr. Gorsche and his colleague Dr. Rob Wedel, are part of a six-member research team looking into how being on call affects Alberta physicians and their families. With the support of the Rural Physician Action Plan (RPAP), the two rural doctors are able to take time away from their practices to attend six SEARCH II (see page 47) training modules. Their commitment requires them to devote half a day a week for the two years it will take them to conduct their research and promote the findings within their health regions. Dr. Maeve O'Beirne, Director of the AHFMR-funded Alberta Family Practice Research Network, based at the U of C's Faculty of Medicine, is also a member of the team.

So far, the group has held focus groups in towns and cities ranging from Taber to Slave Lake, in the six regions they represent, to develop questions for a survey that will be sent to family physicians province-wide. Physical, emotional, psychological, and financial burdens of being on call will be addressed in the survey. Results will be compiled and analyzed in early 2000 and disseminated in a unique way: The group plans to commission a play to illustrate the issue's human aspects. An educational video incorporating the play, will also be developed to help doctors, medical students, and other professionals similarly affected better cope with being on call.

Community-centred health research

Finding out how to advance health in our communities is part of the push for health research expertise outside of urban centres. Factors like geography, prevalent occupations, cultural mix, and income all contribute to a unique health profile for each community in Alberta. Research conducted in communities gives a true picture of health that can be used in that community's healthcare decision-making. Several research networks, institutes, and organizations are helping build the capacity for community health research throughout Alberta.

Alberta player on a world team

The Health Technology Assessment Unit at AHFMR is an international player. Similar units around the world assess global literature on the tools of health care—therapies, devices, treatments—to see what works best. The HTA unit at AHFMR has produced many assessments of technologies ranging from surgery to alleviate Parkinson's tremors to bone density measurement for osteoporosis.

Encouraging research

▶ The Alberta Family Practice Research Network, based at the University of Calgary's Faculty of Medicine, provides research expertise to physicians around the province. AHFMR provides operating funds to the Network. Dr. Maeve O'Beirne, the Director of AFPRN, wants to broaden the use of the Network so that community family physicians—both urban and rural—become the major clients.

▶ The Alberta Consultative Health Research Network, also supported by AHFMR, is headquartered in Calgary's Department of Community Health Sciences. The Network is guided by Dr. Marja Verhoef in Calgary and Dr. Ollie Triska at the University of Alberta. Together, they are building a provincial network of experts and resources to support health researchers throughout the province.

▶ The Institute of Health Economics is a not-for-profit research agency representing a partnership of 15 organizations from government, industry, and universities, including AHFMR. The Institute focuses on health and pharmaceutical outcomes, policy, and economics research.

SEARCH: Tailor-made research for Alberta

When health care was decentralized to 17 health regions in Alberta, one of the important components of each region's business plans was research that would inform decision-making. But many regions did not have the experience to conduct health research in their communities.

AHFMR proposed a unique training program called Swift Efficient Application of Research in Community Health Care (SEARCH) that was tailored to Alberta's healthcare landscape. AHFMR provided $1 million for the first two-year SEARCH training program in 1996, which included a one-of-a-kind computer network to link 23 participants situated all over the province. Two years later, the success of SEARCH was evident in the completion of 90 individual and 6 group projects on research topics designated as priority topics by their health regions. Another indication of success was the popularity of the program: In May 1998, SEARCH II was launched, again with participants conducting research all over the province.

SEARCH I and SEARCH II are operated with the participation of the Regional Health Authorities, the Provincial Mental Health Board, the Alberta Cancer Board, Alberta Health, the University of Alberta, and the University of Calgary.

Injury Prevention Resources

Injury Prevention Plus
http://www.injurypreventionplus.com/main.htm

Alberta Centre for Injury Control & Research
780/492-6019

Child Injury Information Resouces

Health Canada Laboratory for Disease Control
http://www.hc-sc.gc.ca/main/lcdc/web/brch/injury/chrpa.html

Elderly Health Resources

Health for Seniors
http://www.health.gov.bc.ca/seniors.html

Primary Health Care Evaluation Network
http://www.primaryhealth.org/main/evalnet/index.htm

Women's Health Resources

Canadian Women's Health Network
http://www.cwhn.ca/indexeng.html

Women's Health Interactive
http://www.womens-health.com

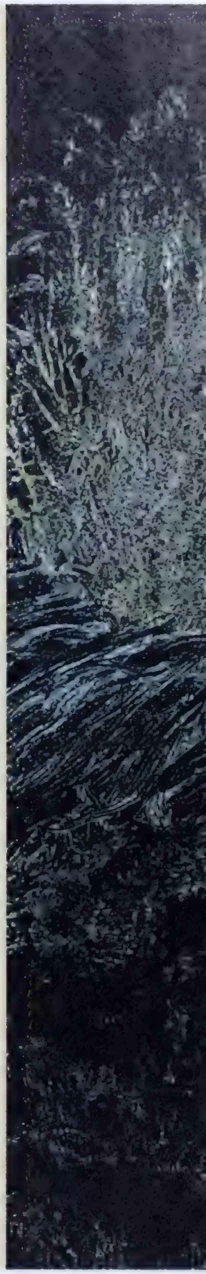
Office of Women's Health
http://www.fda.gov/womens/default.htm

Physician & Researcher Resources

Alberta Family Practice Research Network
403/220-2750

The Alberta Consultative Health Research Network
Toll-free: 1-877-670-4337

Swift Efficient Application of Research in Community Health (SEARCH)
780/423-5727



Researchers mentioned:

Dr. Maeve O'Beirne is based at the U of C and receives support through the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness.

Dr. Marja Verhoef is based at the U of C and receives support through the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness.

Taking it to the limits

"Too many years ago," laughs Dr. Marek Michalak, "As a student in Poland, I was seriously considering a career in professional tennis." As it turns out, the Heritage Medical Scientist still wields a mean racquet in his habitual early morning squash games, but his true calling is biomedical research.

Although we'll never know what the world of tennis lost, his commitment—and that of the "Membrane Group", the other five members of a research group specializing in cell biology—has paid spectacular dividends to the University of Alberta. In early 1999, Dr. Michalak and fellow membrane group members received $5 million, one of the biggest awards to a single research group from the Medical Research Council of Canada. This was from a total of $11 million awarded to the University from MRC.

Dr. Michalak with colleague, fellow squash player and AHFMR researcher, Dr. Luis Agellon

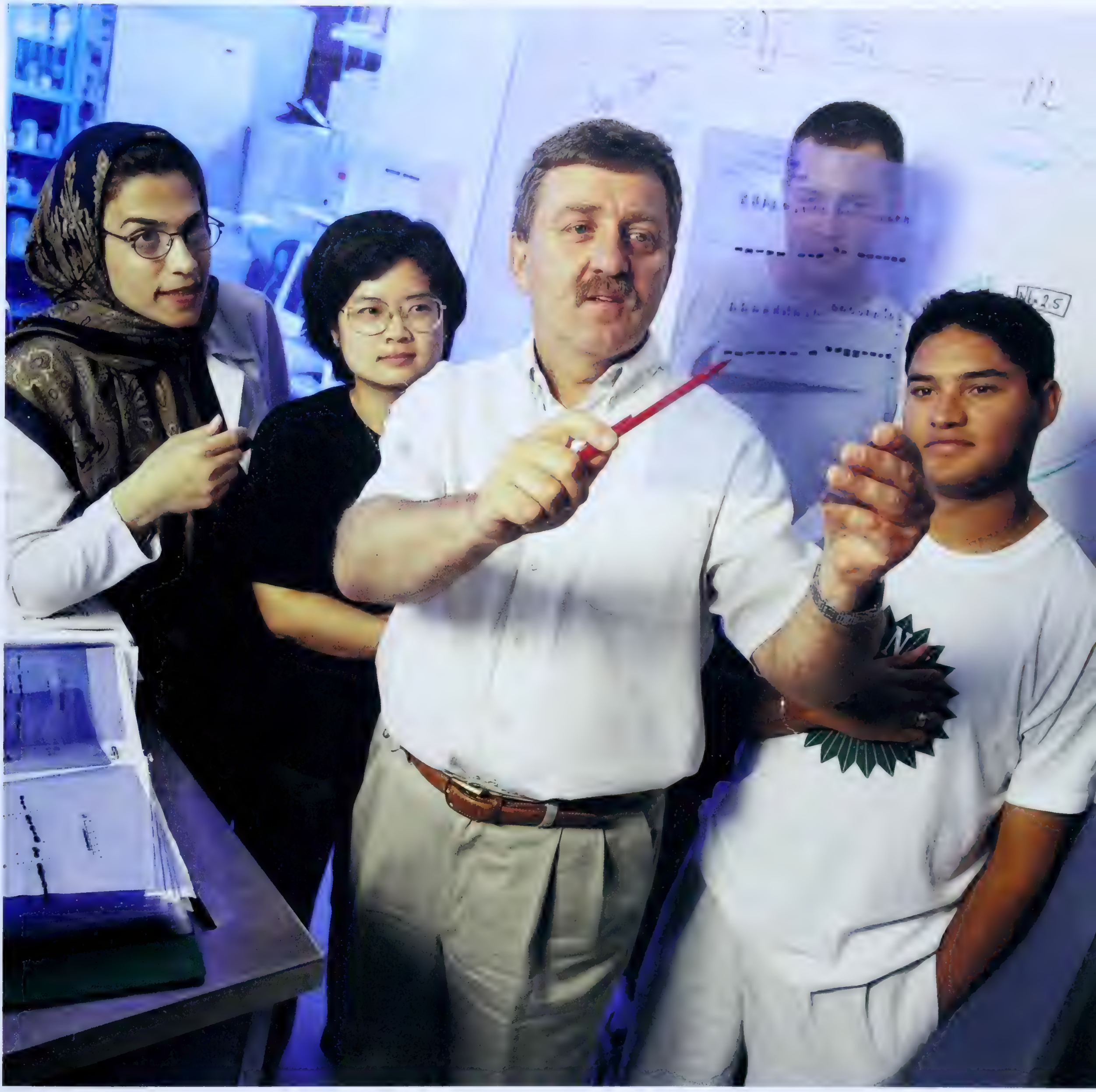
Dr. Michalak attributes the Group's success to AHFMR: Heritage funding enabled his own recruitment from Toronto to the University of Alberta 14 years ago, three other Group members were also recruited to U of A through Heritage, and the other two have received AHFMR funding at some point during their careers. But as crucial as funding is to research, it's really a person's character that Dr. Michalak believes makes or breaks a career in science.

"I had one student in my lab—a straight-9 student who aced every exam—but he couldn't handle life in the lab. He would do experiments, they wouldn't work, and he couldn't comprehend that he was doing something and it wasn't successful right away. He couldn't deal with failure. I realized that in this business you basically fail all the time. You fail for years to discover something that takes ten minutes to do, and then it's over and you can start failing again. If you can't deal with failure, you are really in trouble with science!"

Dr. Michalak has first-hand experience with failure, with listening to instincts, and with those "ten minutes" of success. He describes a decade's worth of his research that focused on the effect on muscle of a particular cell-membrane protein called calreticulin. Everything he tried seemed to indicate that the protein is insignificant in muscle, but his instincts were telling him otherwise. On the verge of closing down the project he asked himself one more question: "What would happen in an organism if the gene that made this protein were deleted?"

"The results were stunning," he recalls. "It turned out muscle was the major thing affected." Further work led to the discovery that, during embryo development, calreticulin is one of the most critical molecules to help the muscle develop properly. When the muscle is fully developed at birth, the protein is no longer needed, so it all but disappears. Even more important, when Dr. Michalak introduced the protein into a mature organism's heart, the result was a severe reaction leading to heart failure and sudden death. What had started out as a "trivial" protein suddenly had enormous implications for heart disease.

"The heart failure we were seeing in our experiments



Dr. Marek Michalak and students
Heritage Medical Scientist at the University of Alberta
Supported by AHFMR for 12 years

with calreticulin resembles very closely a heart condition—idiotypic dilated cardiomyopathy—described by clinicians as an example of disease resulting from viral infection of the heart. In at least one third of patients, this leads ultimately to transplantation or death. Yet we were able to show the same symptoms without the presence of a virus. Our hypothesis is that a virus may have something to do with the gene that produces calreticulin."

Pediatric cardiologists know from experience with many children that by the time they show symptoms of cardiomyopathy, it's too late. The only recourse is transplantation. If Dr. Michalak's work can show a way of intervening early enough to prolong the disease's rapid onset, it would buy more time for the child waiting for an available heart. "Right now, once these kids show symptoms, they have about 12 months to find a heart."

His embrace of the unexpected in his research extends into his collaborations. He describes a fruitful collaboration with Dr. Chris Bleackley—a Heritage researcher and renowned immune scientist who made international headlines with his work on T cells—as starting out with a wedding. "One of his students and one of mine got married. Chris found a new role for calreticulin in the immune system. Surprisingly, there seems to be something in common between how the immune system reacts to stress (infection) and how organs (heart) develop—the 'stress' of making an organ. In a global way, there are many different systems in the body but they use similar genetics and biochemical mechanisms and similar molecules at different times for different processes."

His global approach to science is reflected in the students who vie to work in his lab and those he has already mentored. Former post-doctoral fellows and graduate students are engaged in research, or industry, or teaching in Canada, Europe, and the United States. The international profile of the people he is training includes Japan, China, Iran, Poland, and Ireland, with others coming soon from Germany and Italy. His own story of how he came to Canada is based on the web of connections so common in the scientific world.

"My Ph.D. supervisor in Poland knew David MacLennan at the Best Institute in Toronto, who has mentored a number of outstanding scientists in Canada and throughout the world. So I came to Canada as a post-doctoral fellow. I had the best of both worlds," he says. "My Ph.D. supervisor taught me how to do science well and David also taught me to be competitive, to not be afraid, to go for the cutting edge."

After 25 years in a field that has gone through very difficult times, he still thinks science offers the best of many worlds to young people. "The past ten years have been difficult, but we're now seeing a real investment happening that is wonderful. I tell students that this is really a life without borders. It's very international and the benefits of collaborations and connections all over the world cannot be replaced by salary. I tell my students, 'In science, when you discover something, no one in the world knows about it until you say it.' That's the power of science. That's the joy of it."

AHFMR investment from 1996-99 doubled by Perinatal Research Group

The six scientists in this group have been funded for a total of 59 person years.

Twenty-nine research trainees working in five scientists' labs were AHFMR-funded for a total of $280,000.

$1,900,000	total amount awarded by AHFMR to the six scientists*
$2,100,000	total external funding attracted by group
$4,000,000	total funding of group

*Figures are approximations and are rounded off to the nearest thousand.

Professional resources for researchers and physicians

Healthy Beginnings –
Capital Health Authority, Edmonton
780/413-7995

Calgary Regional Health Authority –
Early Intervention Program
403/569-2100

Giving new life the best chance for health

"Our theme is that perinatal research is for life," says Dr. David Olson, the Head of the Perinatal Research Centre Group, which is housed at the University of Alberta and the Royal Alexandra Hospital.

Dr. Olson started the Group eight years ago, defying standard thinking in university research groups by gathering together top-notch researchers from different faculties, disciplines, and research traditions. The results are impressive: the Group's funding is in the millions of dollars per year and dozens of young scientist-trainees are attracted by the Group's unorthodox and successful collaborations.

Dr. Olson with members of the Perinatal Research Group: Dr. Sandra Davidge, Dr. Jane Mijovic-Kondejewski with baby, and graduate student, Rachel Szilard.

As Dr. Olson explains, the Group's research interests range from bench to bedside. "Not only do we study new life (including total development and birth), but we also study the life-long consequences of pre-term birth and other perinatal insults." About 7% of babies born in Edmonton are pre-term, and about 90% of them survive. But that small percentage of total children accounts for 70% of all childhood illnesses. "Some aspect of being born early results in these babies having lifelong illnesses," explains Dr. Olson.

Several Heritage basic biomedical researchers, as well as researchers supported by the Health Research Fund, are members of the Perinatal Research Centre Group. Nine of the Health Research Fund researchers are from the University of Alberta's Faculty of Nursing.

When every breath is a struggle

▶ When we're healthy, our immune system protects us from innumerable types of micro-organisms—fungi, bacteria, viruses—that co-exist with us.

Dr. Chris Mody

When a person has a deadly disease like AIDS, however, the immune system slowly winds down, unable to fight secondary infections or invasions. A common inhaled fungus called cryptococcus often kills AIDS patients because the gene for clearing the fungus from their body is damaged by the disease. Dr. Chris Mody works with AIDS patients trying to trigger the remaining parts of their immune systems to compensate for functions that are no longer there.

▶ Premature babies born at less than 24 weeks-gestation struggle to breathe. Their undeveloped lungs lack a vital coating called surfactant that both protects delicate tissue and helps maintain air pressure. Animal surfactants can be given, but with the danger of species-transferable diseases, scientists are looking to develop artificial surfactant. Dr. Sam Schürch has developed a tool to measure the effectiveness of artificial surfactants, and he receives surfactant samples from all over the world to test. He also works with another University of Calgary scientist, Dr. Francis Green, to study how efficiently we clear pollutants from our lungs. Their work may have implications in understanding the effect of toxic particles on the rising incidence of asthma and allergies.

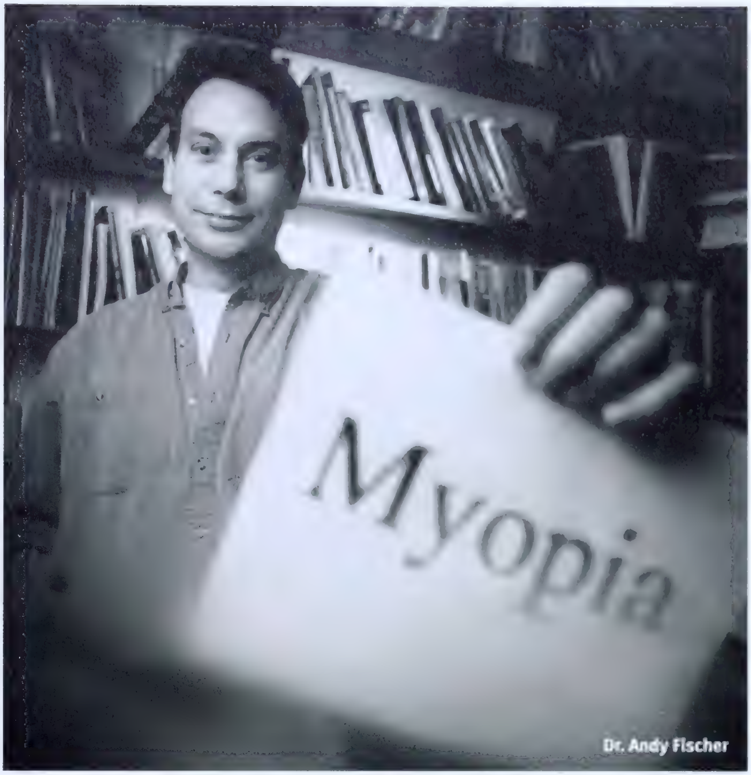
▶ Dr. Carol Adair conducted landmark research that established the connection between second hand smoke and ear infections in children.

▶ Lung scarring can result from toxins, burns, or a number of diseases and conditions, such as lupus. When scarring occurs, the delicate tissue of the lungs stiffens, preventing vital air exchange. Dr. Brent Winston is seeking ways to interrupt the cell signalling involved in one type of lung scar formation—Adult Respiratory Distress Syndrome—that occurs very rapidly, with a very high mortality rate.

▶ One out of eight schoolchildren has asthma, and the rates are rising sharply. That is a health problem that has a costly price tag—nearly $75 million is spent annually in Alberta treating breathing difficulties resulting from asthma. Dr. Patrick Hessel's "Attack on Asthma" research project, coordinated by the Alberta Lung Association, surveyed more than 5000 schoolchildren throughout Alberta to capture current data on asthma rates, as a first step in devising interventions and preventive measures for the disease.

Improving health in early years

When Jane Mijovic-Kondejewski learned she was pregnant, she was unsure of the date of conception and was more than a little anxious about a premature delivery. Happily, baby Matthew was born healthy and right on time. Unlike most expectant mothers, Dr. Mijovic-Kondejewski had first-hand knowledge of what premature birth can do to babies and mothers. A member of the Perinatal Research Centre Group, she is working with the Royal Alexandra Hospital's Department of Obstetrics and Gynecology to study maternal and fetal hormones that stimulate contractions. The team hopes to identify drugs that will prevent preterm labour.



Dr. Andy Fischer

Visionary research

Myopia, also known as near-sightedness, is a lengthening of the eyeball, which causes images to be projected in front of the retina, resulting in blurred vision. Although glasses and laser surgery correct vision, they address the symptoms of myopia, not the causes of excessive eye growth. The signals that trigger eye growth are found in the retina at the back of the eye. Dr. Andy Fischer stumbled upon an amazing discovery in the course of his research into the causes of myopia. While testing certain growth hormones, he found they actually made retinal cells grow again. Now on a Heritage fellowship at the University of Washington, Dr. Fischer is pursuing this new research direction, which raises exciting possibilities about transplantation of living retinal cells into damaged eyes to restore sight.

Dr. Robert Ryan

Lipid research — providing vital links to health

Too much fat in our diets, coupled with sedentary lifestyles and genetics, can lead to heart disease, the number one killer of both women and men in North America. Yet, we need cholesterol and other essential fats, called lipids, to build cells and nerves, make hormones, and send signals. These are basic functions of life, and when they are altered the result can be deadly.

How do lipids function in the body? Heritage scientists at the University of Alberta are trying to answer that question by studying the most basic interactions of lipids and cells. What they are gleaning is providing the first steps for new therapies, perhaps cures, for a number of diseases.

▶ Mice are much more efficient at getting rid of cholesterol than humans are. Dr. Luis Agellon has discovered one possible reason why. The gene in mice that corresponds to the cholesterol-removing gene in humans reacts differently to regulation by lipids. In fact, the human gene doesn't respond well at all to fats in the diet. Dr. Agellon hopes to find ways to trigger the gene in humans that could be used in cholesterol-lowering drugs.

▶ When a patient is tested for cholesterol, doctors assess the levels of good and bad cholesterol. Traditional cholesterol-lowering medicines lower the harmful cholesterol (LDL), but no currently available drug raises the levels of protective, good cholesterol (HDL). HDL helps remove excess cholesterol that accumulates in arteries and causes heart attacks and strokes. Dr. Gordon Francis has found a way of modifying HDL so that it is much more effective at removing cholesterol from cells. A surprising and beneficial side effect of this action is that it also causes a marked increase in HDL levels. His work may yield new approaches to treating and preventing heart disease and stroke by raising HDL levels.

▶ Dr. Dennis Vance discovered a gene that makes an enzyme called PEMT, that in turn, makes a lipid called PC in the liver. Further research had unexpected results: When the gene was eliminated in mice there were no problems until the mice were fed a diet deficient in choline (which is used in another way the body can make PC). Without choline, the mice developed liver failure in three days. Dr. Vance's research showed that the gene is necessary to provide PC in the liver when choline is absent from the diet, for example during starvation.

▶ Dr. David Brindley is working out the signals used by a lipid messenger that lets fat cells bypass insulin to use sugar. His research could bring new insights into insulin resistance, a major health problem for nine out of ten Adult-onset (Type II) diabetics.

▶ Lipids attached to proteins inside the cell function like a zip code. These attached lipids help deliver message-containing proteins to the "right address" in the cell. These proteins control various activities including growth, and cholesterol transport in the bloodstream. Dr. Luc Berthiaume investigates the roles of the various lipids attached to proteins involved in cancer development and heart disease.

▶ Dr. Robert Ryan is studying the effects of special proteins—apolipoproteins—which are equipped to carry lipids around in the bloodstream. When one particular apolipoprotein is mutated, there is a suspected link to Alzheimer's disease.

▶ Dr. Richard Lehner is studying three enzymes that control how a particular lipid is used in the body. Too much of the lipid, called triacylglycerol, causes obesity. Dr. Lehner's research has led to the development of an inhibitor for one of the enzymes that could lead to a drug therapy.

Perinatal and Early Life Resources

Perinatal Research Centre, University of Alberta
HtmlResAnchor http://www.ualberta.ca/PERINATAL

National Parent Information Network
http://npin.org

The National Parenting Centre
http://www.tnpc.com

Call your local public health clinic (listed in the phone directory) for information on local community programs that integrate the Canadian Prenatal Nutrition Program.

Lung Disease Resources

Canadian Lung Association
http://www.lung.ca

Eye Resources

Canadian Association of Optometrists
http://www.opto.ca

Alberta Association of Optometrists
http://www.optometrists.ab.ca

Heritage researchers who are part of the Perinatal Research Group:

AHFMR Senior Scholar Dr. David Olson researches fetal lung development and the biochemical triggers to preterm birth.

AHFMR Scholar Dr. Sandra Davidge studies pre-eclampsia, a potentially life-threatening high-blood- pressure disorder that affects some pregnant women.

AHFMR Senior Scholar Dr. John Greer investigates the biological signals that lead to congenital diaphragmatic hernias, a rare condition that develops in the womb and is often fatal.

AHFMR Medical Scientist Dr. Gary Lopaschuk works with enzymes that may arrest tissue damage after the heart is stopped during heart operations.

AHFMR Senior Scholar Dr. Rick Schulz focuses on how to save heart cells that are affected during massive infections.

AHFMR Scholar Dr. Marek Radomski studies the effects of nitric oxide in pre-eclampsia.

The following Perinatal Research Group members are supported by the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness:

Dr. Bryan Mitchell is using an assessment tool to see how an expectant mother's health, along with intervention and treatment by a doctor, affects newborn health.

Researchers affiliated with the U of A Faculty of Nursing:

Dr. Christine Newburn-Cook is investigating the causes of low birth weight.

Dr. Kathrine Peters is using a special program that assesses premature babies' physical reactions to indicate the individual care they need.

Dr. Carol Estabrooks assesses to what extent research results are used in hospitals.

Dr. Ruth Elliott looks at the role a special caregiving intervention program will play in the development of children at risk.

Dr. Lynne Ray is developing and testing interventions for chronically ill children and their family caregivers.

Dr. Nicole Letourneau is examining social support interventions for children and families at risk.

The following Perinatal Research Group members are AHFMR full-time students in the Faculty of Nursing:

Ms. Jennifer Medves is investigating evidence-based nursing practice in maternity care.

Ms. Vicki Boechler was one of the participants in AHFMR's first SEARCH Program. She is currently studying interactions between fathers and infants.

Ms. Karen Benzies is studying the impact of family environment during a child's early development on the child's behaviour in school.

Other Heritage researchers mentioned in these articles:

Dr. Sam Schürch is an AHFMR Medical Scientist at the U of C.

Dr. Chris Mody is an AHFMR Scholar at the U of C.

Dr. Carol Adair Bischoff is an AHFMR alumna at the U of C.

Dr. Patrick Hessel is a U of A doctor whose "Attack on Asthma" research is supported through the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness.

Dr. Jane Mijovic-Kondejewski is an AHFMR alumna at the U of A.

Dr. Andy Fischer is an AHFMR Post-doctoral fellow at the University of Washington.

Dr. Dennis Vance, Dr. David Brindley, and Dr. Robert Ryan are AHFMR Medical Scientists.

Dr. Luis Agellon is an AHFMR Senior Scholar.

Dr. Luc Berthiaume is an AHFMR Scholar.

Dr. Richard Lehner is an AHFMR Scholar (as of July 1, 1999).

Dr. Gordon Francis is an AHFMR Clinical Investigator.

Taking it to the limits

He doesn't quite fit the typical image of an entrepreneur. He doesn't sit behind an executive desk or wear expensive business suits.

In fact, you're likely to find him in his small, but sunny office in the Heritage Medical Building sporting a well-worn lab coat and comfortable leather slippers. Yet "entrepreneur" is the word Heritage Medical Scientist Dr. Tony Schryvers uses to describe himself.

An "entrepreneur", the Concise Oxford Dictionary states, "undertakes a business or enterprise with chance of profit or loss." Dr. Schryvers explains how the definition applies to him: "As an independent research scientist, you can pursue what you want to pursue as long as you can convince the people with the money that it's worth doing," he says. "Most successful researchers are entrepreneurs because that's what they're doing. They basically have to go out and get the money to conduct their business just like the average small businessperson."

> *"Most successful researchers are entrepreneurs.... They basically have to go out and get the money to conduct their business just like the average small businessperson."*

As a senior scientist with nearly 20 years of grant writing and industry partnering experience, Dr. Schryvers knows what he's talking about. So far, he's garnered almost a million dollars in industry support for his vaccine research. He filed his first patent for receptor-based vaccines over ten years ago. Then he entered a partnership with a major pharmaceutical company to further his research on an experimental vaccine for *Neisseria meningitidis* infection which has proved to work well in animals and has entered Phase l clinical trials in humans. It is based on his discovery that bacteria need iron from the host to grow and survive. Using the iron receptors as a target for the immune system effectively kills the bacteria. Dr. Schryvers' approach has application to a number of different bacteria that cause important infection in humans and animals.

In 1997, Dr. Schryvers received Phase ll funding from AHFMR's Technology Commercialization Program to develop plant-based vaccines. He also has ongoing research and agreements with industry related to human and veterinary vaccine development. With the experience he has gained working in applied research and development, Dr. Schryvers hopes to be able to act as a resource for other colleagues pursuing industry partnerships.

As a young scientist, the strong reputation of the University of Alberta's Department of Biochemistry attracted the Saskatchewan native to Edmonton, where he completed his Ph.D. in biochemistry. In 1984, he obtained his M.D. from the University of Calgary. He received Heritage funding as a graduate student and continues to maintain AHFMR support at the most senior level as a Heritage Medical Scientist at the U of C.

Despite his established background in applied research, Dr. Schryvers vigorously supports the importance of basic research. "Although I am strongly involved in applied research and application, I think you have to have free-wheeling research and a willingness and ability to exploit anything useful that comes from it," he contends. "I also believe that you can have a much greater impact on society as a research scientist. Developing a vaccine for meningitis can have a wide impact and make a big difference in people's lives."

Dr. Anthony Schryvers (holding soccer ball) and members of his lab

Heritage Medical Scientist at the University of Calgary

Supported by AHFMR for 15 years

Dr. Schryvers' post-doctoral supervisor, Dr. Larry Bryan, encouraged in the researcher what has now become his "entrepreneurial" style. He encouraged his students to challenge dogma and ask questions, even if the questions were outside their main field of study, his former student says. "He nurtured in me the idea that researchers have to be willing to take risks and try different approaches to addressing questions."

The Heritage researcher continues to foster this philosophy in the students who work in his lab. "One of my strengths when I came into this area of research is that I wasn't specifically trained in it. I didn't have any preconceived ideas or biases. I came in and did something that they probably said couldn't be done." Spoken like a true entrepreneur.

Infectious Disease Resources

Antibiotic Resistance
http://www.fda.gov/fdac/features/795_antibio.html

http://www.cdc.gov/ncidod/dbmd/antibioticresistance/Default.htm

Virus Resources

Institute for Molecular Virology
http://www.bocklabs.wisc.edu

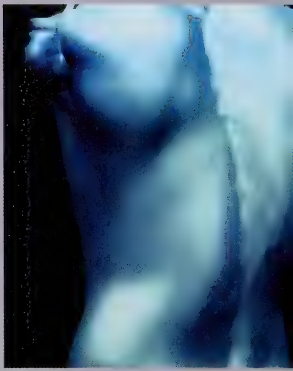
Laboratory Centre for Disease Control (Health Protection Branch)
http://www.hc-sc.gc.ca/hpb/lcdc/hp_eng.html

Joint Injury and Arthritis Resources

The Arthritis Society
http://www.arthritis.ca/home.html

McCaig Centre for Joint Injury and Arthritis Research
http://joint.mccaig.ucalgary.ca/jiarg

Alberta Centre for Injury Control & Research
http://www.med.ualberta.ca/acicr



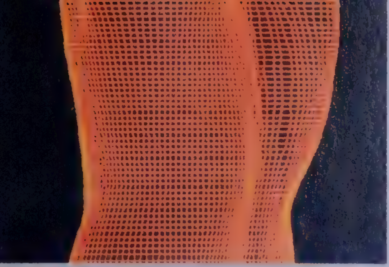
The following investigators receive support through the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness:

Dr. David Hanley is investigating whether lack of sunlight causes Vitamin D deficiencies. His research project is part of a larger study of osteoporosis among 9000 Canadian women and men over 25, funded by MRC. The study of 300 Calgarians will investigate whether there are seasonal causes linked to Vitamin D deficiencies and bone density loss.

Fibromyalgia is a pain disorder with no identifiable cause and no known cure. A study conducted by Dr. Liam Martin will assess the effectiveness of mineral supplements in treating the disorder.

Dr. Raj Rangayyan is developing computer technology and mathematical processes to combat the difficulties related to reading mammograms.

Many other researchers associated with JIARG have also received AHFMR support.



Movement to excellence

AHFMR investment from 1996-99 nearly quadrupled by the Joint Injury and Arthritis Research Group

The eight scientists have been funded by AHFMR for a total of 45 person years.

Thirteen research trainees working in four scientists' labs were AHFMR-funded for a total of $430,000.

$1,500,000	total amount awarded by AHFMR to the eight scientists*
$4,200,000	total external funding attracted by group
$5,700,000	total funding of group

*Figures are approximations and are rounded off to the nearest thousand.

Finding the cause and best treatment for arthritis, a complex and often-crippling condition, and developing innovative techniques to repair debilitating joint injuries suffered by many Albertans, are the goals of an exceptional community of clinicians, basic scientists, and engineers brought together through the U of C's Joint Injury and Arthritis Research Group (JIARG). Based in the McCaig Centre in the Heritage Medical Building in Calgary, the Group is made up of outstanding scientists with backgrounds in areas as diverse as engineering, biochemistry, molecular biology, and orthopedic surgery. Their combined efforts are having a major impact on what is known about the disease.

JIARG is strengthening its human resources even further through a $1.3 million grant from the prestigious Whitaker Foundation in the United States, which will see the establishment of a joint graduate program in biomedical engineering at the U of C and U of A. The goal of the program is to train up-and-coming biomedical engineers to work in the areas of joint injury and arthritis in the province.

AHFMR-supported researchers who are part of the Joint Injury and Arthritis Research Group:

Heritage Scholar Dr. Robert Bray and Dr. Cy Frank, a Heritage Scientist who pioneered knee ligament transplants in Western Canada, use new biomedical techniques to improve healing and prevention of knee problems before they lead to osteoarthritis.

Heritage Clinical Investigator Dr. Paul Salo is investigating whether osteoarthritis is caused by changes in the nervous system due to aging and disease.

Heritage Scholar and molecular biologist Dr. Tim Heslip is using what he has learned about the genetic material of the *Drosophila* fruit fly to identify in humans similar genes involved in the progression of arthritis and joint injury.

Dr. Neil Duncan, the recipient of an AHFMR Independent Establishment Grant, is studying intervertebral discs in the lower back to better understand how they break down and cause problems in some people.

Heritage Senior Scholar Dr. Phyllis LuValle is a new JIARG member who adds her expertise in molecular biology and gene expression to the Group's efforts.

Dr. Ron Zernicke, Chair of JIARG and Dean of Kinesiology, is an expert in biomechanics, the science of body movement.

Dr. Jerome Rattner received AHFMR Technology Commercialization support to develop a screening test for a lupus antigen.

Dr. John Matyas received AHFMR Technology Commercialization support to continue research and development of the glomerular retrieval system used to recover pieces of kidney tissue lost during routine kidney biopsies.

Research to aid defence

▶ Dr. Julie Deans investigates how the body's defence system works against disease and invasion.

Dr. Kamala Patel

Specifically, Dr. Deans is studying the signalling system that cells use to help fight off invading bacteria.

▶ Cell biologist Dr. Kamala Patel's work delves into the molecular mechanisms of the body's immune system and, how they relate to inflammation and common inflammatory diseases such as asthma.

Dr. Patel's basic research is contributing to a better understanding of how white blood cells get to where they are going and could help scientists develop new and better drug therapies for asthmatics.

▶ It is thought that genetics accounts for 50% of the incidence of Type I diabetes, but Dr. Pere Santamaria thinks that the immune system also plays a role in its onset. He is trying to determine the relationship between the genes and the immune system, using models of diabetic and non-diabetic families.

▶ Dr. Michael Surette is investigating what causes individual bacteria to swim in solution and move over certain surfaces in a swarm. He thinks the cell-to-cell signalling involved in swarming may provide clues for developing therapies to treat certain diseases.

▶ Dr. Rakesh Kumar searches for new compounds to stop HIV at its earliest stages. He is also devising compounds that might someday be used to treat a number of herpes viruses. One other area of research for Dr. Kumar is the hepatitis B virus, on which he works in collaboration with Dr. Lorne Tyrrell.

Dr. Tyrrell has been nationally recognized for his groundbreaking work on hepatitis B. His research has recently led to a drug that could potentially save millions of lives worldwide. Dr. Tyrrell's research has been conducted in the Glaxo Heritage Centre at the University of Alberta.

Student prowess in bacterial research

Concern is growing that common infections may eventually become resistant to current antibiotic treatments. Peter Hwang spent four summers in the Calgary lab of Heritage Scientist Dr. Hans Vogel researching lactoferricin, a microbial peptide that has been found to kill bacteria. Pairing the unique

Dr. Walter Maksymowych with patient

properties of lactoferricin with conventional antibiotics may be the ammunition needed to wipe out increasingly resistant bacterial strains. Mr. Hwang's research could one day contribute to the development of a new class of high-potency antibiotics.

Biomedical Engineering Program

▶ The University of Calgary and the University of Alberta were joint recipients in 1997 of a $1.3 million Special Opportunity Award from the Whitaker Foundation, based in the United States.

The award will fund a unique Biomedical Engineering graduate curriculum offered collaboratively between the two universities. Key staff at the two institutions include Dr. Ron Zernicke and Dr. Nigel Shrive at the University of Calgary, and Dr. Peter Allen and Dr. Gary Faulkner at the University of Alberta.

▶ There are over 100 different kinds of arthritis that can affect the lives of Albertans. Dr. Walter Maksymowych's research on arthritis focuses on three forms of the often crippling disorder: ankylosing spondylitis, rheumatoid arthritis and osteoarthritis. Through his University of Alberta laboratory and patient-based research, Dr. Maksymowych is testing the effects of osteoporosis medication he believes may help in the treatment of inflammation and bone thinning.

Researchers mentioned:

Dr. Julie Deans, Dr. Kamala Patel, and Dr. Michael Surette are AHFMR Scholars at the U of C.

Dr. Pere Santamaria is an AHFMR Senior Scholar at the U of C.

Dr. Rakesh Kumar is an AHFMR Scholar at the U of A.

Dr. Lorne Tyrrell is Dean of Medicine at the U of A. His lab at the Glaxo Heritage Centre at the U of A was started with $1million from AHFMR.

Dr. Ron Zernicke is Dean of Kinesiology at the U of C.

Dr. Nigel Schrive, at the U of C is an AHFMR Technology Commercialization Program alumnus.

Dr. Peter Allen at the U of A is an AHFMR alumnus.

Dr. Walter Maksymowych is an AHFMR Scholar at the U of A.

Peter Hwang is an AHFMR alumnus at the U of C.

Discovering connections

Morgan is not your average ten-year-old. A Grade 6 student in a school for gifted kids, he has used his biking prowess to raise a total of $10,000 for his favourite non-profit group, the Southern Alberta Brain Injury Society (SABIS).

> *Six years ago, Dr. Weiss made international headlines and turned conventional thinking in neuroscience inside out with his discovery of brain-stem cells in mammals.*

Morgan was brain-injured seven years ago, and he and his mother, who was also brain-injured in the same automobile collision, struggle daily to cope. In Morgan's case, since the part of his brain that controls behaviour was damaged, he has problems controlling his impulses. Thanks to a supportive environment sought out by his mother—of SABIS, teachers, students and healthcare workers—Morgan is doing very well. But, says his mother, brain cells do not regenerate and recovery is a lifelong process.

Morgan's mom is right—for now—but if Heritage Medical Scientist Dr. Sam Weiss' goals are reached, she hopes to be proven wrong within her lifetime.

Six years ago, Dr. Weiss made international headlines and turned conventional thinking in neuroscience inside out with his discovery of brain-stem cells in mammals. Stem cells, the basic, primitive cells from which all other cells evolve, exist in many tissues in the body. Up to the time of Dr. Weiss' discovery, it was common medical belief that brain cells could not grow, divide, or specialize into nerve cells. He found stem cells in all stages of brain development from the embryo to the adult, and they divided and grew when stimulated with a growth factor.

Dr. Weiss and co-discoverer Dr. Brent Reynolds, with the help of AHFMR's Technology Commercialization Program, founded a company called Neurospheres to further develop stem-cell technology. (Although Neurospheres doesn't exist anymore as a research operation, licensing from its patents continues to provide revenue to the University of Calgary.) The duo envisioned a time when their research would lead to therapies to repair the damage done to brain tissue by stroke, trauma, or disease.

The linking of basic research to clinical application has motivated Dr. Weiss' career since he was an undergraduate. "In my final year at McGill I took a course in neurochemistry from two Canadian legends in the field: Theodore Sourkes and Leonhard Wolfe. They took everything I had assumed to be just sort of test-tube chemistry and showed that this knowledge could be applied to understanding the nervous system. It spurred me on to explore the potential applications of biochemical knowledge toward understanding the brain, the spinal cord, and neurodegenerative diseases."

Dr. Weiss became a Heritage Postdoctoral Fellow in France and there, in 1985, made his first major discovery: a new receptor for glutamate, an important signalling molecule in the brain. The metabotropic glutamate receptor is now one of the hottest areas of drug-discovery focus in the pharmaceutical industry today. "It led me to try and develop new ways of treating neurodegenerative diseases because glutamate, in excess, is thought to kill brain cells. We were experimenting with growth factors in the pursuit of new ways of protecting brain cells from glutamate, and one of the growth factors turned out to be

Dr. Sam Weiss and Morgan, brain injury survivor
Heritage Medical Scientist at the
University of Calgary
Supported by AHFMR for 16 years

the one that makes stem cells divide."

Dr. Weiss' lab is currently embarked on two main research directions. One area is investigating how a specific "family" of genes, known as transcription factors, regulate stem cells enabling them to develop into mature nerve cells. He is collaborating with Dr. Michael Rosenfeld at the Howard Hughes Institute in San Diego who is considered a world leader in transcription factors. With his help, Dr. Weiss has identified a transcription factor that could be critical in pushing an immature nerve cell towards maturity and a permanent stable state.

Other research focuses on finding the master genes for the production of dopamine cells—the principal cells lost in Parkinson's disease—from stem cells. His expertise in the area of neurodegenerative diseases and the applications of stem-cell technology make his lab a magnet for graduate and post-doctoral fellows. He has several trainees who are helping him develop stem cell research models for Huntington's disease, Parkinson's disease, and multiple sclerosis.

Bringing researchers together across international borders and between formerly distinct fields of study is the way of the future as Dr. Weiss sees it. He was instrumental in creating the new Genes & Development Research Group in the University of Calgary's Faculty of Medicine. He also is planning an international collaborative project that involves Dr. Bryan Kolb and Dr. Ian Wishaw at the University of Lethbridge, both eminent in the field of behavioural and restorative neurology.

Dr. Weiss is gearing up to exploit the wealth of information resulting from the Human Genome Project, a global effort to identify the nearly 100,000 genes in the human body that should be complete within two years time.

"I really believe that gene discovery is neither tissue nor species specific, that it's broader than that. New discoveries will be made by not limiting oneself and not focusing too heavily on just where you work or what you work on, but by broadening the perspective to look at genes that are critical in general growth functions. In our case, we're interested in growth of cells in all animals and all tissues. So it could be that the link between the growth of the gut in a worm and the growth of the brain in a mouse may all boil down to the same or very similar transcription factor master switch."

Morgan's mom heard about a presentation Dr. Weiss gave to SABIS members last year. "I am awed by the knowledge that we have such a world-class group of neuroscientists here in Alberta. It gives me great hope."

Children's mental health

Dr. Deborah Dewey and Dr. Marli Robertson with their children. Laura Kaminsky is on far left.

Gastroenterologist and medical researcher Dr. Marli Robertson and psychologist Dr. Deborah Dewey, along with doctoral student Laura Kaminsky, are working in three vastly different research fields to try and help children who suffer from chronic pain.

Dr. Robertson's medical practice includes babies who have a shortened bowel, the result of surgery to correct life-threatening bowel conditions. Her laboratory work focuses on finding ways to speed up the healing process in the bowel. In particular, she studies on how certain enzymes function in the volatile world of the intestine to maintain cell equilibrium and to turn on the cell's response to growth factors.

When children have attention deficit hyperactivity disorder (ADHD), they often have problems in language development—reading and writing. According to research conducted by Dr. Deborah Dewey and Dr. Bonnie Kaplan, the cause of this may not be the ADHD, but poor motor-planning skills, also found in about 30% of kids with ADHD. Dr. Dewey's background in kinesiology, the study of body movement, and neuropsychology, has led to a number of research pursuits involving children and development.

Laura Kaminsky's doctoral studies are focused on the social development of siblings of autistic children. She has found that most of the children in her study have good social and psychological development and, in fact, many report a great admiration for their autistic sibling.

The three researchers are collaborating to study how children cope with pain stemming from a condition called functional recurrent abdominal pain. These children suffer very real, chronic pain without an identifiable physical cause. Help is often offered through psychological support, although it is clear the condition is not caused by stress. The team is assessing different ways affected children cope with pain to see if some of these coping strategies can be used to help children who suffer chronic pain from other illnesses.

Researchers mentioned:

Dr. Marli Robertson is an AHFMR Clinical Investigator at the U of C.

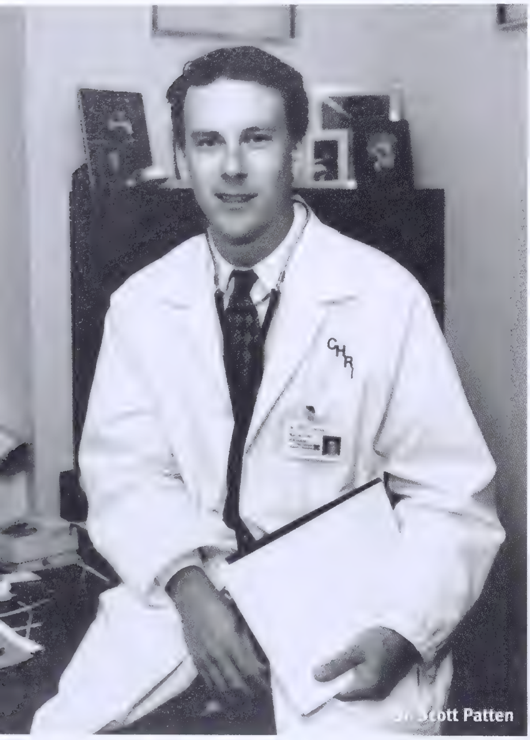
Dr. Deborah Dewey receives support through the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness. She is with the Alberta Children's Hospital in Calgary.

Dr. Bonnie Kaplan receives support through the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness. She is at the U of C.

Laura Kaminsky is an AHFMR doctoral student at the U of C.

Mental Health

▶ It strikes for no apparent reason. Its victims experience extreme anxiety, heart palpitations, profuse sweating, and the desire to escape from wherever they happen to be. Panic disorder, if not treated can lead to phobias—fears that curtail normal activities, so that sufferers hide behind the curtains of life. Panic disorder is thought by scientists, including Dr. Nicholas Coupland, to result from a complex mix of psychological and biological factors. Dr. Coupland is trying to identify what alters in a particular chemical in the brain when people have panic disorder. He has also collaborated with Dr. Jean-Michel LeMellédo in a project that showed changes in the same chemical system in women who suffer severe premenstrual mood changes.


Dr. Scott Patten

▶ Dr. Candace Konnert is conducting pioneering research to identify levels of anxiety and depression in elderly nursing-home inhabitants. If her studies can help caregivers and family distinguish between mental and physical health problems, then appropriate care can be given.

▶ One of the most frightening manifestations of acute mental illness is delirium. Nightmarish auditory and physical sensations can lead to dangerous situations for affected patients, who include psychiatric patients, alcoholics, the elderly, and post-operative patients. Dr. Scott Patten is identifying the risk factors for delirium in order to provide information for early intervention, medication changes, and shortened hospital stays.

▶ Bipolar disorder, also known as manic depression, affects one percent of the population and, indirectly through their families, countless more. For the past 50 years, one of the most effective treatments for bipolar disorder has been lithium, a salt-based chemical, whose exact functioning in the brain is unknown. Dr. Peter Silverstone is trying to decipher how lithium and other mood-stabilizing drugs work on brain cells, knowledge that could lead to further refinement of the drug.

▶ Telehealth, the practice of long-distance medicine, has immediate applications in some branches of medical practice. The delivery of mental health services is one area in which telehealth technology shines, according to a study conducted by AHFMR's Health Technology Assessment unit and SEARCH participant Jennifer Simpson in six regional hospitals. The report showed that both psychiatrists and patients reported a high level of satisfaction with the technology, opening the doors for better delivery of mental health services in Alberta and other areas of Canada.

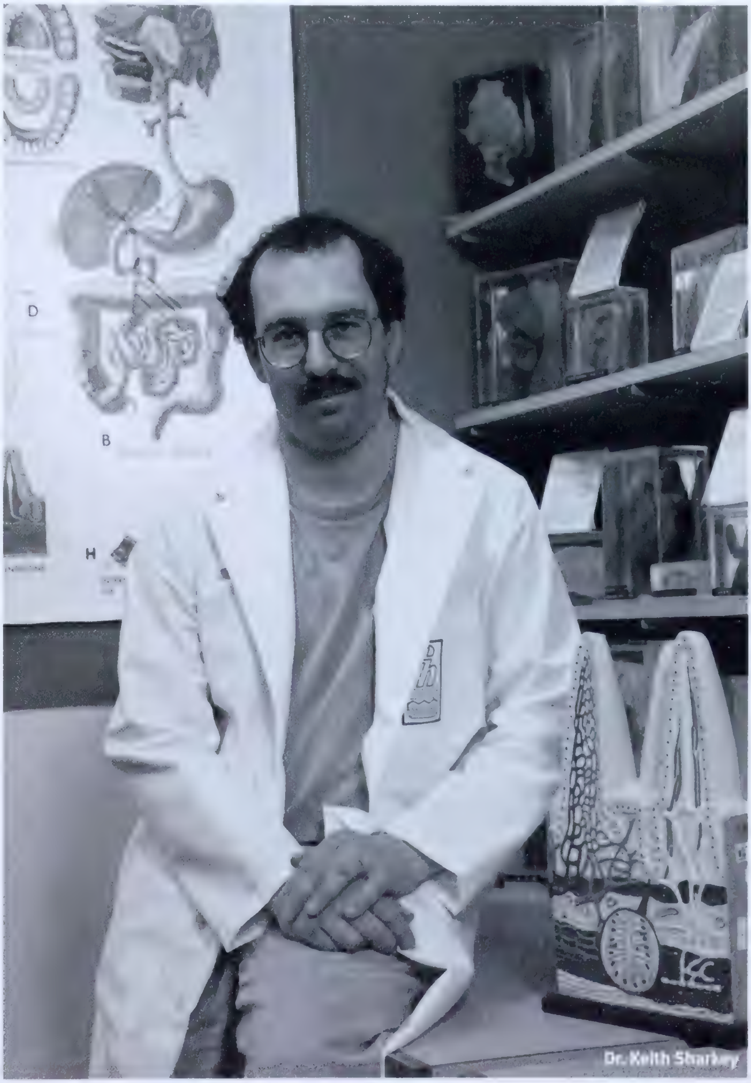
▶ Lethbridge is famous for its wind, the haunting landscape of inverted hills called coulees, and the arresting design of its university, spilling down the hillsides. The University of Lethbridge has an equal claim to fame in its superb behavioural psychology research group, headed by Dr. Bryan Kolb, an internationally acclaimed researcher. Dr. Jeffrey Kleim is a member of Dr. Kolb's department and his research is centred on identifying the mechanisms in the brain that allow recovery from stroke.

Insights into the brain

▶ Dr. Lori Buchanan at the University of Alberta also studies stroke, using the power of magnetic resonance imaging to see details of brain activity generated when stroke patients read using a variety of methods. If she can pinpoint language pathways that are undamaged by stroke, the information may help stroke victims and others suffering brain injury to develop new ways of reading or speaking.

▶ Dr. Sarah McFarlane's basic research may also lead to new information that helps the brain-injured, although she stresses that her focus is not on patients but on the processes that cause nerves to grow and connect. She has focused on a family of growth factors that influence growing nerve cells differently at various stages of development. When completely understood, these important growth factors might play an important part in the quest to regenerate damaged nerve cells.

▶ The term "gut reaction" has just as much to do with the brain as it does with the intestines. Dr. Keith Sharkey's research is providing evidence of the complex interactions between the nervous system and the gastrointestinal tract (gut). Dr. Sharkey studies how inflammation alters activity in the nerves that signal what the gut is doing. By manipulating the nervous system, he hopes to modify intestinal inflammation. His research results may provide a new target for future drug therapies.


Dr. Keith Sharkey

AHFMR brain power

▶ Eight AHFMR researchers were the recipients of the first-ever Neuroscience Canada Foundation awards for outstanding neuroscience research in Alberta. Recipients at the University of Alberta were Dr. Arthur Prochazka, a pioneer in developing electrical devices that help paraplegics move limbs; doctoral student Miguel Martin-Carabello, who studies how the brain controls breathing; and doctoral student Glen Newell, who investigates a brain chemical associated with tranquilizers.

▶ The four University of Calgary awardees are also studying brain function. Dr. Quentin Pittman researches the brain molecules that control such vital body processes as temperature, breathing. Dr. Gaynor Spencer investigates brain cell connections after injury. Doctoral student Pamela Valentine studies how noise damage to the ears affects the brain. Doctoral student Leonie Moorhouse Herx delves into the actions of certain brain cells in patients recovering from brain injury. Dr. John McKenna, a post-graduate fellow from the University of Lethbridge, received his award for his research into how the nervous system changes when recovering from spinal cord injury.

▶ Why does the body sometimes resist the drugs and therapies that are intended to make it well? Doctoral student Glen Newell is trying to solve a piece of this puzzle that involves one of the main receptors for signals in the brain. He's studying how a main chemical brain messenger, called GABA, acts like a key to unlock the receptor gateway in nerve cells, in order to let the nerve cells talk to one another. Many drugs currently target the GABA receptor and if Mr. Newell can identify how GABA activates the receptor, he may be able to provide information for better drugs.

Researchers mentioned:

Dr. Nicholas Coupland and Dr. Jean Michel LeMellédo are AHFMR Clinical Investigators at the U of A.

Dr. Candace Konnert receives support through the Health Research Fund administered by AHFMR on behalf of Alberta Health and Wellness.

Dr. Scott Patten is an AHFMR Population Health Investigator at the U of C who also received support from the Health Research Fund administered by AHFMR on behalf of Alberta Health and Wellness.

Dr. Peter Silverstone is an AHFMR Clinical Investigator at the U of A who also received support from the Health Research Fund administered by AHFMR on behalf of Alberta Health and Wellness.

Dr. Jeffrey Kleim is an AHFMR Scholar at the U of L.

Dr. Lori Buchanan is an AHFMR Scholar at the U of A.

Dr. Sarah McFarlane is an AHFMR Scholar at the U of C.

Dr. Keith Sharkey is an AHFMR Senior Scholar at the U of C.

Miguel Martin-Carabello and Glen Newell are AHFMR doctoral students at the U of A.

Dr. Arthur Prochazka is an AHFMR Medical Scientist at the U of A.

Dr. Quentin Pittman is an AHFMR Medical Scientist at the U of C.

Dr. Gaynor Spencer is an AHFMR Post-doctoral fellow at the U of C.

Pamela Valentine and Leonie Moorhouse Herx are AHFMR doctoral students at the U of C.

Dr. John McKenna is an AHFMR Post-doctoral fellow at the U of L.

Recent Achievements in Neuroscience and Mental Health Research

- Helping to unravel how sound is interpreted by the brain
- Determining how certain drugs such as tranquilizers, act in the brain and why they stop working over time
- Pioneering electrical devices that help paraplegics move limbs
- Information on how the brain controls breathing development
- Tracking delirium in at-risk patients to understand why it happens and how to prevent it
- Testing telehealth, the practice of long-distance medicine using electronic connections between patients in rural areas and specialists in psychiatry
- Insight into how the GABA system may trigger panic, and its links to depression
- New understanding of how changes in female hormones during the mentrual cycle and pregnancy may affect panic attacks in women

Brain Injury

Brain Injury Association of Alberta
Toll-free: 1-800-533-5355
in Calgary: 403/207-5606

Edmonton: The Northern Alberta Brain Injury Society
780/479-1757

Calgary: The Southern Alberta Brain Injury Society
403/521-5212

Vancouver Island Head Injury Society
http://www.bcl.com/vihis/links.htm

Neuroscience

Human Neurological Diseases
http://www.neuroguide.com/neurodis.html

American Academy of Neurology
http://www.aan.com

Mental Illness

Canadian Mental Health Association (Alberta Division)
http://www.alberta.cmha.ca

Canadian Mental Health Association (National)
http://www.cmha.ca

The Clarke Institute of Psychiatry
http://www.clarke-inst.on.ca

Provincial Mental Health Board
http://www.pmhab.ab.ca

Panic Disorder

National Institute of Mental Health
http://www.nimh.nih.gov/publicat/index.cfm

Depression Therapy
http://keytodepression.com

National Institute of Health (Treatment of Panic Disorder)
http://www.webcom.com/bmainc/nihpanic.html

Sharing opportunities

Growing up in Washington State, the thought of wearing a lab coat didn't dawn on young Linda Reha-Krantz.

The teenager never considered research as a viable career option until she took part in a summer program similar to one now offered at the University of Alberta. The WISEST (Women in Scholarship, Engineering, Science and Technology) program gives young women the chance to test their interest in science while working in the lab of a researcher-mentor.

> *"Research is certainly a very rewarding career. It is very satisfying to know that you are on the edge of where knowledge ends and the unknown begins, and are able to advance that edge in some way."*

The Heritage Medical Scientist originally wanted to follow in the footsteps of her high-school biology teacher. "I'm not sure I would have thought about the opportunity to do research without having had that summer experience," Dr. Reha-Krantz reflects. That fateful summer job and support from her teacher steered her toward what is now an established career in genetic research.

Heritage funding and the opportunities a burgeoning province afforded her young family drew Dr. Reha-Krantz to Alberta in the early eighties, allowing her to build a solid base from which to conduct her research and form collaborations with researchers world-wide.

In 1996, an opportune partnership with Dr. Myron Goodman, from the University of Southern California, led to the development of a major improvement on a technique that makes it easier for scientists to detect DNA. The technology was developed with funding from AHFMR's Technology Commercialization Program.

Mentoring

Though she might not realize it, Dr. Reha-Krantz emulates her former biology teacher by actively encouraging young scientists through her own work. Over the past ten years, a number of WISEST students have received crash courses in genetics, studying different mutations in DNA under her tutelage. She has also mentored more than 40 undergraduate and graduate students in the last 20 years. Many of these students have gone on to careers in science. "Research is certainly a very rewarding career," Dr. Reha-Krantz notes. "It is very satisfying to know that you are on the edge of where knowledge ends and the unknown begins, and are able to advance that edge in some way."

Making science accessible is a philosophy that is reflected in her teaching style. Dr. Reha-Krantz builds a communications seminar into her fourth-year genetics course that she hopes will turn students into science ambassadors. In it they learn skills that help them convey scientific concepts in language that non-scientists can understand.

An explanation of her own research comes across simply and clearly: "Each time a cell divides, the genetic information held in DNA molecules is copied. Highly efficient enzymes called DNA polymerases carry out this important copying function," she explains. "DNA polymerases have the amazing ability to replicate (reproduce) DNA with both great speed and accuracy." She is

Dr. Linda Reha-Krantz
(and 1999 WISEST student, Denise Ng)
Heritage Medical Scientist at the
University of Alberta
Supported by AHFMR for 19 years

determining how DNA polymerases accomplish this task. "It is important to understand the mechanism of DNA replication, because an error in DNA replication can cause human diseases, such as cancer. DNA replication can also be used as a target for anti-viral drugs that inhibit the viral DNA polymerase, but not the human DNA polymerase," she says.

One of her most important recent discoveries is determining why DNA polymerases make a particular error known as "simple repeats" when replicating DNA. The DNA polymerase seems to "slip" when copying the repeated DNA and make extra copies of the repeat. This type of DNA replication error can have serious consequences, including loss of gene function. For example, if the gene that controls cell growth is affected, then that loss of function could result in tumor formation.

Building on a further belief that "knowledge is power," Dr. Reha-Krantz believes that everyone should have a science education. "The public need to educate themselves about the current genetic revolution," she opines. "Science and research have an impact on every part of our lives—from the genetically-altered foods that we purchase and consume to making decisions about our health and our family's health."

1997 recipient of the McLeod Scholarship Rachel Szilard (left) with Mrs. Barbara McLeod and Dr. Matthew Spence

Rachel Szilard

Outstanding doctoral student Rachel Szilard was awarded the 1997 Lionel E. McLeod Health Research Scholarship in Edmonton.

Ms. Szilard works in the Department of Cell Biology at the University of Alberta studying how proteins in peroxisomes (compartments found in the cells of many organisms, including humans), act in yeast. These compartments help the body break down and use fats, and are essential for life in humans. Babies born with severe deficiencies in peroxisomal functions usually do not live beyond their first year. The knowledge gained from working with peroxisomes in yeast may lead to a treatment for genetic diseases in humans in the future.

Ms. Szilard will continue her research at the Hospital for Sick Children in Toronto. She hopes to integrate basic research and clinical medicine in her work.

A legacy for health research

Building a foundation for research excellence was not only a job, but a joy for Dr. Lionel McLeod, AHFMR's first President and CEO. His legacy of providing opportunities that enable young researchers-in-training to thrive, continues through the annual Dr. Lionel E. McLeod Health Research Scholarship, established in his memory in 1992.

The award is given each year to an outstanding student at the University of Alberta, Calgary, or British Columbia for full-time research that is relevant to human health.

David Dozois

Dr. David Dozois was the 1996 winner of the Dr. Lionel E. McLeod Health Research Scholarship.

As a Heritage-supported doctoral student at the University of Calgary, he studied the thought processes of people with clinical depression. Dr. Dozois is trying to uncover how negative thinking develops in depression and how it may be altered with treatment. His research may someday explain why some people remain depressed while others recover.

Karin Dymond

1998 award recipient Karin Dymond is a student in the combined MD/MSc joint-degree program in the Faculty of Medicine at the University of Calgary. Her studies in the Department of Community Health Sciences are focused on the economic cost of childhood injury and specific injury-prevention strategies, including the use of bike helmets. She is examining the cost and effectiveness of using education, subsidy, or legislation to increase public use of such protective devices.

WISEST

Each summer young women in Edmonton get a chance to explore their interest in science and research through the WISEST (Women in Scholarship, Engineering, Science and Technology) program based at the University of Alberta.

Each summer since 1992, AHFMR has supported a WISEST student to work in the lab of a Heritage-funded researcher.

During the summer of 1996, Jiao Yang learned about adaptive mutation in Dr. Susan Rosenberg's lab. In 1997, Bonnyville high-school student Allison Sandemeyer worked alongside cancer researcher Dr. Linda Pilarski. Dr. Linda Reha-Krant gave a crash course in genetics to Eva Cheung in 1998 and to Denise Ng in 1999.

WISEST Mentor – Dr. Michelle Arnot

Traditionally, science has been seen as a male-dominated field. But up-and-coming female scientists like Dr. Michelle Arnot are helping to change this perception. Not only is Dr. Arnot pursuing her own career with the Science Alberta Foundation, she's acting as a mentor as part of the WISEST program. Exploring every career option is one message Dr. Arnot hopes the young female students she mentors will put into practice.

Participants in the WISEST program

Heritage Media Fellowship Program: Bringing science to the public

Enhancing the quality of science coverage and fostering relationships between the scientific community and the media is the philosophy behind the AHFMR's Media Fellowship Program. The 12-week program provides opportunities for one medicine, science or engineering student at the University of Calgary and the University of Alberta to spend a good part of their summer working as reporters, researchers, or production assistants with a television or radio station or major newspaper in Alberta.

HYRS: Offering a unique summer research experience

Up to 30 exceptional high-school students from all over Alberta with a fascination for science will have the chance to work in the lab of a Heritage researcher as part of the new Heritage Youth Researcher Summer program (HYRS). Starting

Melanie Bodnar, a 1998 Media Fellow

Rafique Virani, a 1997 Media Fellow

in summer 2000, the HYRS program will open up a world of opportunities to students, giving them hands-on experience with some of the most exciting biomedical and health research happening in the province.

Regional Science Fairs

AHFMR maintains its commitment to ensuring a strong future for research and education in Alberta through its participation in the province's six regional science fairs. Every spring, regional winners receive a plaque and $500 from the Foundation to go toward a trip to the Canada-Wide Science Fair.

ATA science conference

A good science education in the formative years can steer young students toward a later career in science or research. For the past two years, the AHFMR has provided support to the annual fall conference of the Alberta Teachers' Association Science Council. The Council is the professional organization for the province's science teachers.

In the past, featured speakers have included Dr. Kamala Patel from the University of Calgary, who spoke about the role of white blood cells in helping the body to defend itself against foreign invasion or inflammatory reactions, and University of Alberta researcher Dr. Rachel Wevrik, who explored advances in genetics.

Cheryl Wellington and Caren Helbing

Dr. Cheryl Wellington and colleague Dr. Caren Helbing, teamed up to conduct a pilot study that addressed the employment concerns of post-doctoral fellows (PDFs). They hope their Heritage-supported survey and registry of Canadian post-docs working at home and abroad will raise awareness about issues of major concerns to PDFs, such as career prospects and job benefits.

Participants in the 1999 Canada-Wide Science Fair

Canada-wide Science Fair

AHFMR continued to help foster the next generation of scientists as a sponsor of the Canada-Wide Science Fair held in spring 1999 in Edmonton. More than 1000 visitors visited the 700 competitors and their outstanding science projects. AHFMR president Dr. Matt Spence announced the Foundation's new Heritage Youth Researcher Summer program at the event's opening ceremonies.

Educational Networks

Industry Liaison Office (ILO)
http://www.ualberta.ca/~ind

University Technologies International Inc. (UTI)
http://www.uti.ca

Edmonton Regional Science Council
http://www.connect.ab.ca/~xdr/ersfc/sf_index.html

Alberta Teacher's Association (ATA)
http://www.teachers.ab.ca

Science Council of the ATA
http://www.atasc.ab.ca/index.htm

WISEST
http://www.awsn.com/WISEST/wisest.html

Alberta Centre for Well Being
780/453-8692

http://www.health-in-action.org/Well-Being

Health in Action
http://www.health-in-action.org

HYRS
http://www.ahfmr.ab.ca

Researchers mentioned:

Dr. Susan Rosenberg is an AHFMR alumna.

Dr. Linda Pilarksi receives support from AHFMR's Technology Commercialization Program. She is at the Cross Cancer Institute.

Dr. Linda Reha-Krantz is an AHFMR Medical Scientist at the U of A.

Dr. Michelle Arnot is an AHFMR mental health research alumna at the U of A.

Dr. Kamala Patel is an AHFMR Scholar at the U of C.

Dr. Rachel Wevrick is an AHFMR Scholar at the U of A.

Dr. Cheryl Wellington is an AHFMR Post-doctoral Fellow at the U of C.

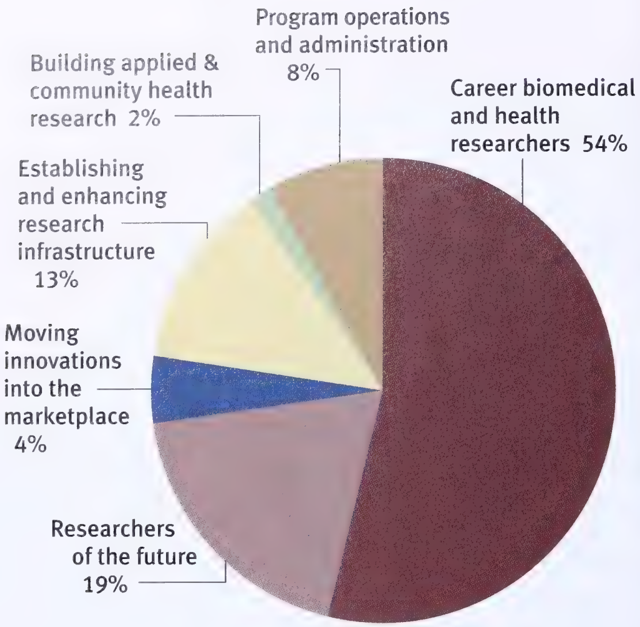
INVESTMENTS IN EXCELLENCE

AHFMR, and all that it has achieved, makes me proud to be an Albertan. It has made Alberta a center of excellence by funding only the best in biomedical and health research. It is immensely satisfying to say to the world: "Alberta's abundant natural resources include oil, wheat, and a top-notch biomedical and health research community." It's equally gratifying to know that AHFMR is a wonderful example of a wise investment that will pay enormous dividends for the health of Albertans for generations to come.

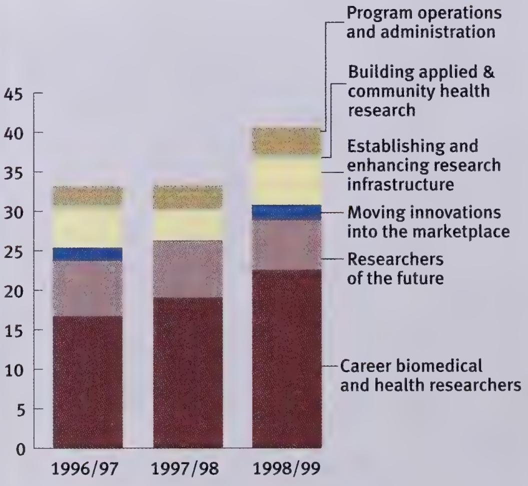
– Premier Ralph Klein

In support of excellence:

$108,277,772 invested directly into research from 1996 – 1999



Total Program Spending 1996 – 1999

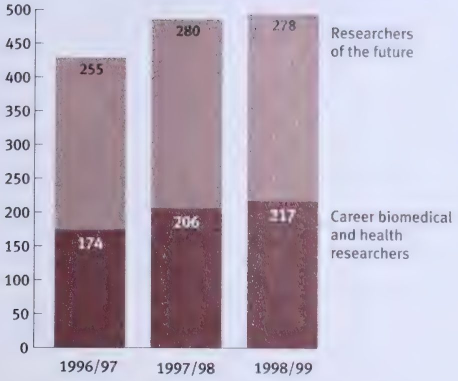


Comparative Spending by Year
($ million)

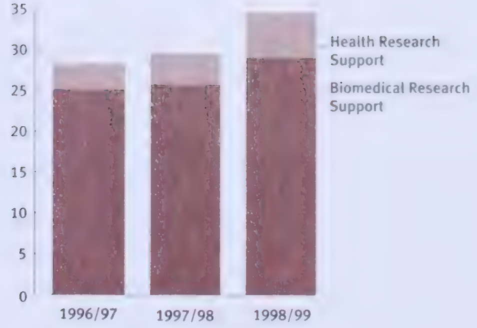
Financial Summary (Combined, Unconsolidated)*

	1996/97	1997/98	1998/99
Revenue	$ 31,709,473	$ 36,608,461	$ 41,534,139
Grants & Awards	29,959,652	30,813,930	36,422,383
Program Operation & Administration	3,296,410	3,482,325	4,299,636
Excess of revenue over expenditure	$ (1,546,589)	$ 2,312,206	$ 812,120

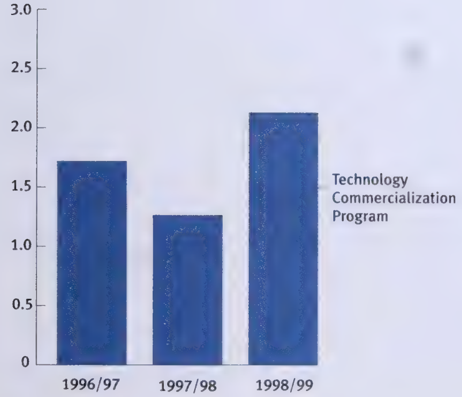
*The above does not include the Alberta Foundation for Health Research.



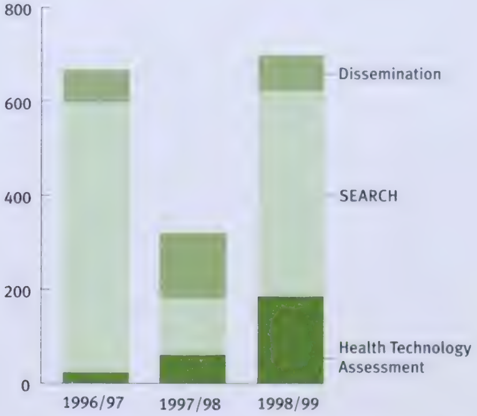
NUMBER OF AHFMR RESEARCHERS



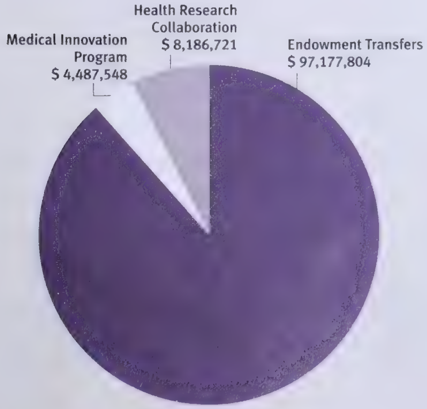
COMPARATIVE SPENDING ON HEALTH & BIOMEDICAL RESEARCH
($ million)



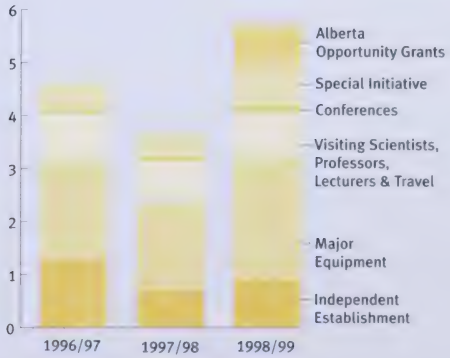
MOVING INNOVATION INTO THE MARKETPLACE
($ million)



BUILDING APPLIED & COMMUNITY HEALTH RESEARCH
($ thousand)



COMBINED FUNDING SOURCES 1996 – 1999



ESTABLISHING AND ENHANCING RESEARCH INFRASTRUCTURE
($ million)

What is our endowment?

The Alberta Heritage Foundation for Medical Research Endowment Fund was established in 1980 to finance the objectives of the Foundation—to establish a long term program of medical and health research in the Province. The Fund operates under the authority of the Alberta Heritage Foundation for Medical Research Act. The initial investment was $300 million.

How is it managed?

The investment policy was developed over a number of years by Alberta Treasury in cooperation with AHFMR Board. The investment policy takes into account the expected conditions in the capital markets, the need for prudent investments, and a sustainable longer term spending program by the Foundation. The investment strategy under this policy is managed by the Investment Management Division of Alberta Treasury. The fund contains a diversified holding of Canadian investments along with equity investments in a number of international markets.

How do we decide how much we need to support our programs each year?

AHFMR management develops long range projections, based on Trustee decisions about maintaining current programs and developing new ones. These projections reflect the cost and number of investigators for each program, related costs and the anticipated value of the endowment. Annual budgets are then developed from this long range projection.

Why do actual expenditures sometimes vary from the budget?

Budgets are based on estimates of quality and number of applications for programs and the results of the review process. Actual expenditures may vary from the budget, depending on the quality and number of applications received and approved, and the number of awards accepted. (Excellence is the primary criteria for funding proposals.) In addition, the Foundation responds to needs as they arise in the community and unforeseen opportunities may result in increased spending.

How do we determine how much to transfer from the endowment to cover our budget?

Foundation management works with Treasury in developing long term investment forecasts and strategies to ensure sufficient cash to fund current operations, while maintaining the value of the endowment by providing sufficient reinvestment of income to ensure future commitments can be met. To provide this balance between current needs and long term goals, the Trustees have adopted a guideline for how much can be transferred each year.

This guideline recognizes that annual income to the endowment could vary drastically, depending on the performance of financial markets in which investments are made. To protect the programs of research from suffering dramatic cutbacks should there be years of significant poor returns, the guideline has two components.

The suggested maximum transferable to the Foundation from the Fund in any year is 70% of the previous year's expenditures, plus 30% of 5% of the opening balance of the endowment. This is a variation of the commonly used 5% rule for endowments which states that, to fund current programs and maintain the potential to fund into the future, only 5% of the value of an endowment should be spent annually.

What is the investment strategy for the endowment?

Due to these relatively high cash requirements to fund annual expenditures, the portfolio is structured to generate a high level of current income with a high degree of certainty. The current portfolio provides for the spending requirements plus growth to cover inflation, with a reasonable margin of safety. In order to generate this income, Treasury has developed a target asset mix for investments in short term, fixed income and equities. These investments are managed approximately 80% directly by Treasury and 20% by international and US managers.

How is Fund performance evaluated?

The Investment Management Division Strategy Committee of Alberta Treasury regularly reviews and benchmarks asset classes, and monitors the performance of fund managers, Treasury meets regularly with Foundation management, and reports fund performance to AHFMR Trustees.

How does the AHFMR decide who to fund?

All final decisions about people and projects supported by AHFMR are made by the Trustees, who weigh the mandate to support a balanced program of research that meets standards of excellence against available income, considering that a portion of it must be added to the endowment to conserve purchasing power for the future.

Who advises the Trustees?

The AHFMR Board of Trustees and executive rely on advice from people in the international, national, and provincial medical research and health communities. Members of the AHFMR Scientific Advisory Council advise on major applications and policy decisions related to research. Other scientists and stakeholders in research, education and health serve on AHFMR committees or as consultants. The Foundation has 13 standing peer review committees and a number of advisory committees for its various programs.

How are applications for funding evaluated?

AHFMR follows the established procedure of evaluating applications by a peer review system. This means applications are judged and rated by other researchers who have esteemed knowledge in the field of the applicant and related areas. Applications are assessed by external reviewers who may be working in any part of the world, and by members of internal AHFMR committees with representatives from Alberta and other North America universities. The committees then forward their recommendations to the Trustees.

How do successful candidates receive their funding?

Researchers funded by the AHFMR are recruited in cooperation with the university, hospital or other organization where the researcher will conduct his or her research. Applications are submitted through the host organization and when the researcher is supported by AHFMR, he or she becomes an employee of the host organization, not AHFMR, although AHFMR pays salary and other support.

What are AHFMR's funding programs?

Heritage Medical Scientists

Heritage Medical Scientists are internationally recognized for their contributions to science. This award encourages the recruitment and establishment of senior medical scientists who provide leadership in Alberta's scientific community. This award is for five years and renewable.

Heritage Senior Medical Scholars

This award assures the continued recruitment and establishment of exceptional investigators in areas relevant to medical and health research. Candidates must hold an M.D., D.D.S., D.V.M., Ph.D. or the equivalent and have an established record of excellence in independent research over several years as a faculty member. The candidate must also show an interest in training Alberta's future research scientists. This five year award is nonrenewable.

Heritage Medical Scholars

Heritage Medical Scholars are investigators who have recently completed their postdoctoral research training and demonstrate the ability to initiate and conduct independent as well as collaborative research. Heritage Medical Scholars exhibit a desire and ability in training future research scientists. This nonrenewable five year award ensures the continuing growth of Alberta's scientific community.

Heritage Clinical Investigators

Clinical Investigatorships allow clinically qualified investigators, holding an M.D. or D.D.S. and full-time academic appointments in a sponsoring institution, further research training and experience assisted by competitively funded basic or clinical researchers. Clinical investigators must have completed two to three years of supervised medical research training. This three-year award is renewable and may be extended for another three years. This award plays an important role in linking basic research to patient-based research and patient care.

Heritage Population Health Investigators

The Heritage Population Health Investigator encourages the recruitment and establishment of well trained health investigators in Alberta. The development of skilled investigators in the fields of population health research, quantitative and population sciences, health services research, social and behavioural sciences and the humanities will establish a centre of excellence for these fields in Alberta. Applicants who have recently completed post M.D. or Ph.D. research training, but who have not yet established an independent research record are eligible for this three year renewable award. This award provides investigators with the opportunity to further their research experience with the aid of a mentor.

Independent Establishment Grants for New Investigators

Independent Establishment Grants are awarded to new investigators whose salaries are not funded by the Foundation. The grant aids new investigators by providing equipment, material and technical assistance that allows them to achieve their goals and increase their research productivity.

Fellowships

Heritage Medical Research Fellowships provide qualified candidates interested in pursuing a career in medical or health related research, with full-time and part-time postdoctoral training in research in any area of medical science relevant to the aims of the Foundation. Candidates must be sponsored by a faculty supervisor and must demonstrate high academic standing and research ability.

Heritage Clinical Fellowships

The Heritage Clinical Fellowship Program provides individuals who hold an M.D. or D.D.S. degree and have completed or are near completion of subspecialty clinical training with the opportunity to pursue a career in health related or clinical research. Applicants must be sponsored by a faculty member who has a record of productive research and agrees to act as the Clinical Fellow's supervisor. Applicants are required to undertake a minimum of two years of full-time research.

Heritage Health Research Career Renewal Awards

The Heritage Health Research Career Renewal Award provides an opportunity for Alberta faculty members, demonstrating interest in clinical or health research, to acquire rigorous training in epidemiology, biostatistics, psychosocial sciences or clinical experimental methods and design. Upon entrance into the program, the investigators are part of a chain reaction that leads to the increased development of clinical and health research activities and the design of patient-based or population-oriented research in Alberta. This award is renewable.

Studentships

The Foundation provides full-time, part-time and summer Studentships in the area of medical and health research. Full-time and part-time Studentships are available for students who are either working towards professional health related degrees or who are interested in pursuing a career in medical or health related research. Summer Studentships provide the opportunity for students with exceptional academic records to participate directly in medical or health related research in Alberta. This program encourages students to consider formal training and a career in health research.

Dr. Lionel E. McLeod Health Research Scholarship

The scholarship was established in the memory of Dr. Lionel McLeod, who was head of Endocrinology at the U of A, Dean of Medicine at the U of A and the founding President of the Alberta Heritage Foundation for Medical research from 1981-1990. The award is given each year to an outstanding student at the Universities of Alberta, Calgary or British Columbia for full-time research that is relevant to human health.

Grants for Major Equipment

Major Scientific Equipment grants allow the university, on behalf of investigators, to purchase the necessary equipment that is essential to maintaining a high quality of research.

Institutional Support Programs

Institutional Support programs aid Alberta's research community in accessing the most up-to-date information and technical developments in medical and health related research. Programs such as the Visiting Lecturer and Travel Funds, Heritage Visiting Professorships, Heritage Visiting Scientists, Infrastructure Grants, Conferences and Workshops and Local Workshops, Retreats or Planning Sessions provide important information and resources necessary to the continuing development and conduct of modern health research in Alberta.

Technology Commercialization (TC) Program

The Technology Commercialization Program funds the commercialization of medically related innovations so that new technology can aid in improving healthcare. The program promotes research/industry collaboration. Technology Commercialization provides funding in three phases for commercially promising projects that do not fall under the mandate of traditional medical research funding agencies and are not developed adequately to attract outside investors. The program also receives funding by a provincial government Medical Innovation Program grant.

Health Research Fund

The Health Research Fund (HRF) was formed by the administrative integration of the Health Services Research and Innovation Fund (HSRIF) and the Mental Health Research Fund (MHRF), both initially established by Alberta Health. Since November 1995, these funds have been administered by the Foundation (AHFMR) through a five-year contract with the government called the Health Research Collaboration. The creation of the Health Research Fund is a direct result of a broad consultation which took place with many individual Albertans and Alberta organizations with an interest in health research. It is intended to provide funding for relevant, high quality health research across the entire spectrum of research areas including mental health research, health services research, population health research and health technology assessment research. This research is essential to sustain the goals of the Health Research Agenda developed by AHFMR through the broad consultation and deliberation of its Health Research Advisory Committee.

Community Health Research Visiting Lecturer Program

Community Health Research Visiting Lecturer awards provide an opportunity to assist Alberta organizations in attracting outstanding health researchers to the province. These visiting lecturers and/or consultants will broaden and enrich the research experience of investigators, administrators and/or trainees by enabling them, individually or in groups, to discuss their health research with the visiting lecturer awardee.

Community Health Research Travel Grant Program

Community Health Research Travel Grants are intended to enhance the quality of health research in Alberta by facilitating contacts between Alberta health researchers, as well as with their national and international colleagues.

AHFMR Opportunity Fund

The purpose of the AHFMR Opportunity Fund (AOF) is to provide an additional opportunity to Alberta institutions (universities and regional health authorities) to develop internationally competitive health research in the province. The AOF is intended to address partnership opportunities for research funding that are not already available through AHFMR's current programs and which require a contribution to funding from other partners.

MD/Ph.D. Trainees

The objective of the program is to provide exceptional candidates, interested in pursuing a career as Clinician Scientists, the opportunity to study for the MD and the Ph.D. degrees simultaneously. The Foundation support is complementary to the formal MD/Ph.D. programs at the University of Alberta and the University of Calgary.

1998-1999 MEMBERSHIP

AHFMR Advisory Committees

Health Research Advisory Committee

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Calgary, Alberta

Dr. Ursula Dawe
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Technology Commercialization Applications Advisory Committee

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Alberta Health Collaboration Advisory Committee

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Clarke Institute of Psychiatry

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Ms. Debbie Phillipchuk
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Drumheller, Alberta

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University of Alberta

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University of Calgary

Dr. George Wyse
University of Calgary

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University of Ottawa

Dr. Garth Bray
McGill University

Dr. Harold Cook
Dalhousie University

Dr. Stephen Lye
Mt. Sinai Hospital

Dr. Grant Pierce
University of Manitoba

Dr. Ken Rosenthal
McMaster University

Dr. Keith Tanswell
Hospital for Sick Children

Dr. David Thomas
National Research Council

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McGill University

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University of British Columbia

Dr. John Schrader
University of British Columbia

Dr. Stephen Sims
University of Western Ontario

Dr. Clifford Stanners
McGill University

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University of Alberta

Dr. Jonathan Lytton
University of Calgary

Dr. Anthony Schryvers
University of Calgary

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University of Calgary

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University of Alberta

Dr. Susan Lees-Miller
University of Calgary

Dr. Brenda Leskiw
University of Alberta

Dr. Sergio Pellis
University of Lethbridge

Dr. Michael Walter
University of Alberta

Success rates for trainee and researcher competitions

For its senior personnel awards competitions and for the Health Research Fund, AHFMR received 831 external reviews of applications which were considered by51 members of 6 review committees who advised the Foundation on these programs. Applications for Trainee awards were considered by 36 members of 4 review committees.

Results are expressed as number of applications received / number of applications approved; followed by the percentage of successful applicants.

	1996/97		1997/98		1998/99	
Clinical Investigators (new)	4 /3	75%	6/4	67%	8/4	50%
Clinical Investigators (renewal)	3/3	100%	3/2	67%	3/2	67%
Scholar (new)	15/8	53%	24/14	58%	23/14	61%
Scholar (Clinical Investigator To Scholar)	3/3	100%	2/1	50%	2/2	100%
Independent Establishment	3/2	67%	5/3	60%	7/5	71%
Senior Scholar (new)	6/5	83%	6/4	67%	4/2	50%
Senior Scholar (Scholar to Senior Scholar)	6/4	67%	7/5	71%	8/4	50%
Scientist - new					3/3	100%
Scientist - new (Senior Scholar To Scientist)	10/5	50%	5/3	60%	4/3	75%
Scientist (renewal)	7/4	57%	8/7	88%	8/7	88%
Health Research Senior Scholar	1/0	0%	2/1	50%	3/2	67%
Health Research Scholar					2/1	50%
Health Research Independent Establishment Grant					1/1	100%
Population Health Investigator (new)	5/2	40%	6/3	50%	10/5	50%
Population Health Investigator (renewals)					5/4	80%
Part-time Fellows	3/3	100%	6/4	67%	1/1	100%
Clinical Fellows	15/8	53%	14/7	50%	15/9	60%
Fellows	128/37	29%	110/35	32%	100/32	32%
Students	182/60	33%	181/61	34%	197/68	35%
Part-time Students	2/1	50%	4/3	75%	3/1	33%
Major Equipment	48/26	54%	31/19	61%	43/35	81%
Health Research Fund	31/19	61%	15/7	47%	51/25	49%
Mental Health Students	8/1	13%	15/6	40%	21/4	19%
Summer Students	384/189	49%	366/182	50%	381/208	55%
TOTALS	864/383	44%	816/371	45%	903/442	49%

"Trainee applications/awards include Biomedical, MD/Ph.D. and Health Research."

Funding details of the Technology Commercialization Program

In 1996/1997, funding was provided in four areas: Drugs, Internship/Training, Medical Research Technologies and Non-Drug Therapies for a total of $1,115, 300.

In 1997/1998, the dollar amount increased 59% to $1,778,730. The projects were funded in six areas: Diagnostics, Drugs, Health Informatics, Internship/Training, Medical Devices and Medical Research Technologies.

In 1998/99, the dollar amount increased 4% to $1,854,015. Funding was provided in seven areas: Diagnostics, Drugs, Health Informatics, Internship/Training, Medical Devices, Medical Research Technologies, Non-drug therapies.

*Includes university spin-out companies who applied independently.

	1996/97		1997/98		1998/99	
Technology Commercialization Program	12/5	42%	49/28	57%	30/15	50%

AHFMR Personnel Awards

Currently implemented personnel as of March 31, 1999

Heritage Clinical Investigator

Todd J. Anderson, MD
Faculty of Medicine, Department of Medicine, University of Calgary
Systemic Nature Of Endothelial Dysfunction

Robert B. Bell, MD
Faculty of Medicine, Department of Clinical Neurosciences, University of Calgary
The Role Of Chemokines And Their Receptors In Delayed Type Hypersensitivity Mediated Inflammatory Demyelination In The Central Nervous System

K. Ming Chan, MD
Faculty of Medicine & Dentistry, Department of Physcial Med & Rehabilitation (Division), University of Alberta
Interventions To Rescue The Decline Of Human Whole Muscle And Motor Unit Function In Aging, Post-Polio Syndrome And Amyotrophic Lateral Sclerosis

Rajni Chibbar, MD, Ph.D.
Faculty of Medicine & Dentistry, Laboratory Medicine & Pathology, University of Alberta
Estrogen And Progesterone Receptor Isoforms In Human Fetal Membranes, Decidua And Myometrium Around The Time of Parturition

Max J. Coppes, MD, Ph.D.
Faculty of Medicine, Department of Oncology, University of Calgary
Mutational Analysis Of The WT1 And WIT1 Promotor Region In Wilms Tumor

Nicholas J. Coupland, MD
Faculty of Medicine & Dentistry, Department of Psychiatry, University of Alberta
Flumazenil In Panic Disorder And Agoraphobia

H. Dele Davies, MD
Faculty of Medicine, Department of Pediatrics, University of Calgary
Population Based Study Of Invasive Group B Streptococcal Infections And Cohort Study Of Maternal GBS Immunity In Alberta

Gordon A. Francis, MD
Faculty of Medicine & Dentistry, Department of Medicine, University of Alberta
Tyrosyl Radical-Mediated Oxidation Of High Density Lipoprotein

Jean-Michel Le Mellédo, MD
Faculty of Medicine & Dentistry, Department of Psychiatry, University of Alberta
Influence Of Administration Of Female Gonadal Hormones On Panic Symptoms Induced By Pentagastrin In Female Panic Disorder Patients

Daphne J. Mew, MD, Ph.D.
Faculty of Medicine, Department of Surgery, University of Calgary
Gene Therapy In Mesothelioma

Ronald B. Moore, MD, Ph.D.,
Faculty of Medicine & Dentistry, Department of Surgery, University of Alberta
Preclinical PDT Studies With Second Generation Photosensitizers

Allan G. Murray, MD
Faculty of Medicine & Dentistry, Department of Medicine, University of Alberta
The Function Of CD95 (fasR or APO-1) Expressed On Vascular Endothelial Cells

Christopher Power, MD
Faculty of Medicine, Department of Clinical Neurosciences, University of Calgary
Molecular Mechanisms Of HIV-1 Envelope Mediated Neurodegeneration

Ronald R. Read, MD, Ph.D.
Faculty of Medicine, Department of Microbiology & Infectious Diseases, University of Calgary
Transport And Antibiotic Delivery In Stenotrophomonas Maltophilia, A Multiresistant Gram-Negative Nosocomial Pathogen

Marli A. Robertson, MD
Faculty of Medicine, Department of Pediatrics, University of Calgary
Cellular Responses Of Intestinal Crypt Cells To Growth Factors And Secretory Stimuli

Paul T. Salo, MD
Faculty of Medicine, Department of Surgery, University of Calgary
Faculty of Neurobiology Of Joint Aging And Degeneration

Peter H. Silverstone, MD
Faculty of Medicine & Dentistry, Department of Psychiatry, University of Alberta
Effects Of Lithium On The Phosphoinositol Cycle In Patients With Mood Disorders

Mark G. Swain, MD
Faculty of Medicine, Department of Medicine, University of Calgary
Cytokine-Neuroendocrine Interactions In Cholestatic Liver Injury: Neuroendocrine Regulation Of Inflammation

Irene E. Wanke, MD, Ph.D.
Faculty of Medicine, Department of Medicine, University of Calgary
Regulation Of Hepatic Gene Expression In Diabetes Mellitus

Brent W. Winston, MD
Faculty of Medicine, Department of Medicine, University of Calgary
TNFa Signal Transduction And Its Role In The Induction Of IGF-1 Gene Transduction

Heritage Population Health Investigators

Timothy A. Caulfield, LLM
Faculty of Law, Health Law Institute, University of Alberta
Legal Issues In The Allocation And Utilization Of Genetic Services: A Model For The Analysis Of Health Care Policies And Reform

Linda S. Cook, Ph.D.
Faculty of Medicine, Department of Community Health Sciences, University of Calgary
Combined Hormone Replacement Therapy And The Risk Of Breast Cancer

William A. Ghali, MD
Faculty of Medicine, Department of Medicine, University of Calgary
Evaluation Of Hospital Mortality And Complication Rates After Coronary Artery Bypass Surgery In Western Canada

Jeffrey A. Johnson, Ph.D.
Faculty of Pharmacy, Institute of Pharmaco-Economics, University of Alberta
Valuation Of The Euroqol And SF-12 And Predictive Capabilities In A Longitudinal Health-Related Quality Of Life Assessment Of Albertans

Colin Macarthur, MD, Ph.D.
Faculty of Medicine, Department of Pediatrics, University of Calgary
A Population Based Evaluation Of The Representativeness Of Emergency Department Data On Childhood Injury

Tara K. MacDonald, Ph.D.
Faculty of Arts & Sciences, Department of Psychology & Neuroscience, University of Lethbridge
Alcohol Intoxication And Health-Risk Behaviours: Understanding And Reducing The Coincidence Of Unsafe Sex And Alcohol Intoxication

Lynn M. Meadows, Ph.D.
Faculty of Medicine, Department of Family Medicine, University of Calgary
The Perceived Health And Health-Related Experiences Of Midlife Women

Scott B. Patten, MD, Ph.D.
Faculty of Medicine, Community Health Sciences, University of Calgary
An Evaluation Of The Impact Of Selection Bias On Case-Control Studies Of Major Depression Using Clinical Subjects

Maria E. Suarez-Almazor, MD, Ph.D.
Faculty of Medicine & Dentistry, Department of Public Health Sciences, University of Alberta
Mortality, Morbidity And Long-Term Institutionalization After HIP Fracture

Heritage Medical Scholars

John D. Aitchison, Ph.D.
Faculty of Medicine & Dentistry, Department of Cell Biology & Anatomy, University of Alberta
Macromolecular Transport Through The Nuclear Pore

Alan N. Bateson, Ph.D.
Faculty of Medicine & Dentistry, Department of Pharmacology, University of Alberta
Regulation And Modulation Of GABA A Receptor Expression

David J. Bennett, Ph.D.
Faculty of Rehabilitation Medicine, University of Alberta
Recovery Of Motoneuron Function After CNS Injury

Luc Berthiaume, Ph.D.
Faculty of Medicine & Dentistry, Department of Cell Biology & Anatomy, University of Alberta
Dynamic Protein Palmitoylation In Cellular Signaling And Targeting

Andrew P. Braun, Ph.D.
Faculty of Medicine, Department of Pharmacology & Therapeutics, University of Calgary
Molecular Analysis of Ca2+ -Activated K+ Channel Structure and Function

Robert C. Bray, MD
Faculty of Medicine, Department of Surgery, University of Calgary
Vascular And Mechanical Adaptations After Surgery

William J. Brook, Ph.D.
Faculty of Medicine, Department of Biochemistry and Molecular Biology, University of Calgary
Molecular Mechanisms Of Limb Development

Christopher B. Brown, MD
Faculty of Medicine, Department of Medicine, University of Calgary
Complexes And Complexities: Studies Of The Receptor For The Hematopoietic Cytokine GM-CSF

Lori L. Buchanan, Ph.D.
Faculty of Science, Department of Psychology, University of Alberta
Phonological Processing In Language Impaired Populations

Brian Burke, Ph.D.
Faculty of Medicine, Department of Cell Biology & Anatomy, University of Calgary
The Nuclear Pore Complex And Nucleocytoplasmic Transport

Joseph R. Casey, Ph.D.
Faculty of Medicine & Dentistry, Department of Physiology, University of Alberta
Mechanism And Interactions Of Anion Exchange Proteins

Sui R. (Wayne) Chen, Ph.D.
Faculty of Medicine, Department of Biochemistry and Molecular Biology, University of Calgary
Structure, Function And Regulation Of Ryanodine Receptors In Smooth Muscle

Sandra T. Davidge, Ph.D.
Faculty of Medicine & Dentistry, Department of Obstetrics & Gynaecology, University of Alberta
Sex Steroids And Vascular Function

Julie P. Deans, Ph.D.
Faculty of Medicine, Department of Biochemistry and Molecular Biology, University of Calgary
Molecular Analysis Of The Multimeric CD20 Complex On B Lymphocytes

D. Moira Glerum, Ph.D.
Faculty of Medicine & Dentistry, Department of Medical Genetics, University of Alberta
Synthesis And Assembly Of Cytochrome Oxidase

J. N. Mark Glover, Ph.D.
Faculty of Medicine & Dentistry, Department of Biochemistry, University of Alberta
The Structure Basis Of The Association And Nucleic Acid Binding Of Transcription Factor Complexes

Paul E. Grundy, MD
Department of Molecular Oncology, Cross Cancer Institute
Identification And Assessment Of Pathological Significance Of Additional Wilms Tumor Loci

Tim Heslip, Ph.D.
Faculty of Medicine, Department of biochemistry and Molecular Biology, University of Calgary
In Vivo Role Of Proteoglycans And Glycosaminoglycans In Growth Factor Signalling

Anthony K. Ho, Ph.D.
Faculty of Medicine & Dentistry, Department of Physiology, University of Alberta
Multiple Receptor Regulated Cyclic Nucleotides: Post-Receptor Mechanisms

May Ho, MD
Faculty of Medicine, Department of Microbiology & Infectious Diseases, University of Calgary
Cellular Immune Responses In P. Falciparum Malaria

Tom C. Hobman, Ph.D.
Faculty of Medicine & Dentistry, Department of Cell Biology & Anatomy, University of Alberta
Protein Trafficking Between The Endoplasmic Reticulum And Golgi

Katherine M. Kavanagh, MD
Faculty of Medicine & Dentistry, Department of Medicine, University of Alberta
The Importance Of Alterations In The Passive Properties Of Myocardial Conduction

Timothy J. Kieffer, Ph.D.
Faculty of Medicine & Dentistry, Department of Medicine, University of Alberta
Leptin Regulation Of Beta-Cell Function And Glucose Homeostasis

Alan F. Kingstone, Ph.D.
Faculty of Science, Department of Psychology, University of Alberta
Brain Mechanisms Of Overt And Covert Orienting

Norman M. Kneteman, MD
Faculty of Medicine & Dentistry, Surgery, University of Alberta
Rejection Of Allotransplanted Pancreatic Islets: Prevention, Early Diagnosis, And Treatment

Gregory S. Korbut, Ph.D.
Faculty of Medicine & Dentistry, Department of Surgery, University of Alberta
Neonatal Porcine Islet Grafts For Human Transplantation: Promoting In Vitro Growth And Co-Transplantation With Sertoli Cells

Rakesh Kumar, Ph.D.
Faculty of Medicine & Dentistry, Department of Medical Microbiology & Immunology, University of Alberta
Design And Evaluation Of Novel Antiviral Agents For Human Immunodeficiency Virus And Herpes Virus Infections

Dennis Y. Kunimoto, MD
Faculty of Medicine & Dentistry, Department of Medical Microbiology & Immunology, University of Alberta
Prevention Of Myocobacterial Infections

Samuel S. Lee, MD
Faculty of Medicine, Department of Medicine, University of Calgary
Membrane Studies In Experimental Cirrhotic Cardiomyopathy

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Vasomotor Mechanisms Of Renal Afferent And Efferent Arterioles

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Molecular Regulation Of Na/Ca Exchanger Function

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Mechanisms Of Acute Radiation-Induced Intestinal Dysfunction

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The Role Of Bacteria In Modulating Intestinal Permeability And Inflammation In The IL-10 Gene Deficient Mouse

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Antigen Processing Genes In Ankylosing Spondylitis

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Molecular Mechanisms Of Visual System Development

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Physiology Of Intestinal Inflammation

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The Immune Response To Cryptococcus Neoformans In AIDS

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Age-Dependent Determinants Of Memory Function And Synaptic Plasticity

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Molecular Mechanisms Of Eosinophil Rolling

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Structure-Based Mechanisms Of Cytosolic Chaperonins And Virulence-Associated Surface Proteins

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Role Of Nitric Oxide In Platelet Function In Normal And Pathological Pregnancies

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The Role of the SRC Family Protein-Tryosine Kinase, HCK in Hematopoietic Cells

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Clinical Trials And Health Outcomes Research In Cardiovascular Disease

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The Effect Of Interferon Alpha 2B On The Biology Of Human Hypertrophic Scars

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Control Of Exocytosis By Intracellular Messengers

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Neuroendocrine Control Of Adrenocorticotropic Hormone (ACTH) Secretion

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Identification Of The Molecular Basis Of Iridogoniodysgenesis

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Organization And Regulation Of Imprinted Genes On Proximal Human Chromosome 15

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Detection Of Vascular Pathology With Transient 3D Magnetic Resonance Angiography

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Human Neutrophil Leukosialin (CD43): Characterization And Functional Significance Of Shedding

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The Role Of Integral Membrane Proteins In The Organization Of The Nuclear Pore

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Molecular Determinants Of Calcium Channel Pharmacology

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Characterization Of A Reverse Transcriptase Encoded By A Group II Intron

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Peptides And Opioids In Peripheral Nerve Injury

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Regulation Of Plasma And Bile Lipid Homeostasis

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Synaptic Plasticity In The Retina: Presynaptic Ion Channels At The Photoreceptor Synapse

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Characterization Of Parathyroid Hypertensive Factor

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Neuroprotective Efficacy Of BDNF And GDNF In Vivo: A Molecular Characterization

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Structure/Function Relations Of Voltage-Gated K+ Channels In Vascular Smooth Muscle

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Respiratory Muscle Compensation, During REM Sleep and Wakefulness, With Diaphragm Paralysis Or Spinal Cord Injury

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Improving Pancreatic Islet Graft Survival By Transfer Of Genes Encoding Immunomodulatory Proteins Into Donor Islets

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The Role Of Ubiquitin Dependent Proteolysis In Cell Proliferation

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Integrated Physiological Response To Acute Hypoxemia In Newborns During Postnatal Maturation

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Ion Exchangers Of Heart Sarcolemma

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Spatial And Temporal Heterogeneity Of Repolarization In Hypertrophy And Congestive Heart Failure

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Diaphragm-Phrenic Nerve Development And The Pathogenesis Of Congenital Diaphragmatic Hernia (CDH)

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Regulation Of Protein Phosphatases -1 And -2A By Natural Product Toxins And Reversible Phosphorylation

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TCR-Activated CD8 Binding In T Cell Adhesion And Response

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Structure And Regulation Of Smooth Muscle

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Polymorphonuclear Leukocyte-Endothelial Cell Interactions: The Role Of Nitric Oxide

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DNA Dependent Protein Kinase In DNA Repair, Viral Infection And Apoptosis

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Regulation Of Fatty Acid Oxidation In The Heart By Acetyl CoA Carboxylase

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Regulation of growth in transformed and senescing cells

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T-Cell Tolerance Versus Genetic Resistance To Spontaneous Autoimmune Diabetes

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Molecular Characterization Of The Structure & Function Of Bacterial Receptors For Transferrin & Lactoferrin

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Molecular Regulation Of Transcription And Chromatin Assembly In Yeast

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Physiological And Pathophysiological Roles Of Nitric Oxide And Peroxynitrite In The Heart

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Molecular Genetic Dissection Of The RAS Signaling Pathway

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Cellular And Molecular Mechanisms Underlying Target Cell Selection And Specific Synapse Formation In A Model System

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Optimization Of An Engineered Bacillus Subtilis Expression System And Its Application To Produce Redesigned Thrombolytic Agents

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Mechanisms Of Process Extension And Myelin Formation By Oligodendrocytes

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Investigation Of Mammalian CAP And CAP2

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Characterization Of Neural Plasticity-Related Phosphoproteins

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Regulation Of Expression Of The Ether-a-go-go Potassium Channel

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Temporal Coding In Auditory Cortex. Effects Of Maturation And Induced Plastic Changes.

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Genetic Analysis Of Several Common Complex Disorders

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The Mechanisms Of Scar Remodeling

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Structure, Function And Regulation Of Ion Channels

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Src-Family Kinases: Function, Regulation And Involvement In Cancers

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Functional Recovery after Central and Peripheral Nerve Injuries.

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Synaptic And Non-Synaptic Control Of Neuronal Excitability

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Development Of The Digestive Tract Of The Nematode Caenorhabditis Elegans

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Calreticulin And Endoplasmic Reticulum Signaling

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Physiological And Pharmacological Studies Of Peptides In Brain

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Mutational And Biochemical Studies Of DNA Polymerases

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Neural Control Of Breathing: Fundamental And Applied Aspects

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B Lymphocyte Selection And Development In The Ileal Peyer's Patch

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Structure And Function Of Amphipathic Exchangeable Apolipoproteins

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Structure And Function Of The Retinal Rod Na-Ca+K Exchanger And Guanylyl Cyclase

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Structure Function Relations Of Alveolar And Airway Surfactant

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Genetic Studies Of Bacterial Plasmids, Campylobacter And Helicobacter

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Cardiac, Pulmonary, And Vascular Determinants Of Left Ventricular Filling

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NMR Studies Of Regulatory And Metal Ion Binding Proteins

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The Pathogenesis Of NSAID-Induced Gastric Mucosal Injury

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Regulation Of Smooth Muscle Contraction By Protin Kinase C And The Thin Filament-Associated Protein, Calponin

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Neurogenesis By Central Nervous System Stem Cells

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Mechanisms Of Cardiac Defibrillation

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Regulation Of Apolipoprotein AI Gene Expression

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Cellular And Molecular Pathogenic Mechanisms For The Induction Of Insulin-Dependent Diabetes Mellitus And Its Possible Prevention

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Molecular Physiology Of Nucleoside And Amino Acid Transporter Proteins

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Determinants Of Spinal Degenerative Findings A Methodologic And Epidemiologic Investigation With Twin Using MPI & DEXA

Major funding partners

The Alberta Heritage Foundation for Medical Research has granted more than $570 million to support health research in Alberta. The Foundation and the Alberta research community relies heavily on the contributions of many partners to build and sustain health research in the province. It is estimated that for every Heritage dollar invested, AHFMR researchers attract $2-3 in outside funding.

A major funding partner in the Heritage health research enterprise in Alberta is the federal government though its major granting agencies: the Medical Research Council of Canada, The National Science and Engineering Research Council, the Social Sciences and Humanities Research Council, the National Health Research Development Program of Health Canada, the Canadian Health Services Research Foundation, the Canada Foundation for Innovation, and Industry Canada.

The Government of Alberta through a number of ministries, health regions, departments, and programs is also a significant partner in AHFMR's endeavours to develop the health research capacity provincially.

The University of Alberta, the University of Calgary, and the University of Lethbridge are key partners with AHFMR in the realization of health research excellence in the classroom, laboratory and at the bedside.

Voluntary funding agencies represent the hope of millions. Their contributions to the work of AHFMR funded researchers are helping to turn hope into realization. The Canadian Heart and Stroke Foundation, the Juvenile Diabetes Foundation, the National Cancer Institutes of Canada and others are valuable allies and agents for better health.

Pharmaceutical companies through the Pharmaceutical Manufacturers Association of Canada or individually are committed to investing in the excellence that AHFMR-funded research delivers.

International funding partners increasingly contribute to Heritage-funded research and include the Whitaker Foundation, the National Institutes of Health, the Wellcome Trust, and many other agencies.

To these partners and to all teachers, politicians, members of the media, and the public whose interest in, and support of, Heritage health research activities have helped us spread the story of AHFMR successes, we thank you and look forward to working with you in the years to come.

Alberta Heritage Foundation for Medical Research

CONSOLIDATED FINANCIAL STATEMENTS

March 31, 1999

AUDITOR'S REPORT 94

CONSOLIDATED STATEMENT OF FINANCIAL POSITION 95

CONSOLIDATED STATEMENT OF REVENUE AND EXPENSE 96

CONSOLIDATED STATEMENT OF CHANGES IN NET ASSETS 97

CONSOLIDATED STATEMENT OF CASH FLOWS 98

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS 99

AUDITOR’S REPORT

To the Trustees of the Alberta Heritage Foundation for Medical Research

I have audited the consolidated statement of financial position of the Alberta Heritage Foundation for Medical Research as at March 31, 1999 and the consolidated statements of revenue and expense, changes in net assets, and cash flows for the year then ended. These financial statements are the responsibility of the Foundation’s management. My responsibility is to express an opinion on these financial statements based on my audit.

I conducted my audit in accordance with generally accepted auditing standards. Those standards require that I plan and perform an audit to obtain reasonable assurance whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation.

In my opinion, these financial statements present fairly, in all material respects, the financial position of the Foundation as at March 31, 1999 and the results of its operations and the changes in its financial position for the year then ended in accordance with generally accepted accounting principles.

Peter Valentine
FCA
Auditor General

Edmonton, Alberta
June 25, 1999

CONSOLIDATED STATEMENT OF FINANCIAL POSITION

March 31, 1999

(THOUSANDS OF DOLLARS)

	1999	1998
ASSETS		
CASH	$3,434	$3,843
RESTRICTED CASH	5,649	6,212
ACCOUNTS RECEIVABLE	22	19
ADVANCES AND PREPAID EXPENSES	40	45
CAPITAL ASSETS (NOTE 4)	586	737
DEFERRED PENSION COSTS (NOTE 5)	73	37
	$9,804	$10,893
LIABILITIES AND NET ASSETS		
ACCOUNTS PAYABLE AND ACCRUED LIABILITIES	$2,138	$1,277
ACCRUED RETIREMENT ALLOWANCE (NOTE 5)	184	134
DEFERRED LEASE INDUCEMENT	40	58
CAPITAL LEASE OBLIGATION (NOTE 6)	55	117
DEFERRED CONTRIBUTIONS (NOTE 7)	5,948	8,204
	8,365	9,790
NET ASSETS (NOTE 8)	1,439	1,103
	$9,804	$10,893

The accompanying notes are part of these financial statements.

CONSOLIDATED STATEMENT OF REVENUE AND EXPENSE

FOR THE YEAR ENDED MARCH 31, 1999

(THOUSANDS OF DOLLARS)

	1999			1998
	OPERATIONS	OTHER PROGRAMS (NOTE 9)	TOTAL	TOTAL
REVENUE				
TRANSFERS FROM ENDOWMENT FUND (NOTE 3)	$ 36,000	$ –	$ 36,000	$ 32,000
AMORTIZATION OF DEFERRED CONTRIBUTIONS (NOTE 7)	–	5,287	5,287	4,183
DONATIONS (NOTE 9)	–	–	–	602
INTEREST	227	31	258	151
RECOVERIES ON TECHNOLOGY COMMERCIALIZATION (NOTE 10)	12	–	12	13
OTHER	8	–	8	273
	36,247	5,318	41,565	37,222
EXPENSE				
GRANTS AND AWARDS				
PERSONNEL	18,586	–	18,586	16,342
TRAINING	5,649	–	5,649	6,066
HEALTH RESEARCH	3,377	–	3,377	1,785
OTHER	4,823	4,487	9,310	6,621
	32,435	4,487	36,922	30,814
PROGRAM OPERATION				
ADVISORY AND PEER REVIEW	385	222	607	472
SEARCH PROGRAM	438	–	438	222
OTHER EXPENSES	–	210	210	128
RESEARCH CONTRACTS	–	(2)	(2)	43
OTHER INITIATIVES	35	–	35	13
	858	430	1,288	878
ADMINISTRATION				
OFFICE ADMINISTRATION	1,630	877	2,507	2,105
COMMUNICATION AND EDUCATION	224	–	224	337
PLANNING AND GOVERNANCE	288	–	288	166
	2,142	877	3,019	2,608
	35,435	5,794	41,229	34,300
EXCESS (DEFICIENCY) OF REVENUE OVER EXPENSE	$ 812	$ (476)	$ 336	$ 2,922

CONSOLIDATED STATEMENT OF CHANGE IN NET ASSETS

for the year ended March 31, 1999
(THOUSANDS OF DOLLARS)

	1999			1998
	INVESTED IN CAPITAL ASSETS	UNRESTRICTED	TOTAL	TOTAL
BALANCE AT BEGINNING OF YEAR	$ 602	$ 501	$ 1,103	$ (1,819)
EXCESS (DEFICIENCY) OF REVENUE OVER EXPENSE	–	336	336	2,922
PURCHASE OF CAPITAL ASSETS	100	(100)	–	–
DISPOSAL OF CAPITAL ASSETS	(25)	25	–	–
AMORTIZATION OF CAPITAL ASSETS	(216)	216	–	–
LEASE FINANCING	25	(25)	–	–
REPAYMENT OF CAPITAL LEASE OBLIGATION	61	(61)	–	–
BALANCE AT END OF YEAR	$ 547	$ 892	$ 1,439	$ 1,103

CONSOLIDATED STATEMENT OF CASH FLOWS

for the year ended March 31, 1999

(THOUSANDS OF DOLLARS)

	1999	1998
OPERATING ACTIVITIES:		
CASH RECEIVED FROM OPERATIONS	$ 36,278	$ 33,039
CASH RECEIVED FROM MEDICAL INNOVATIONS PROGRAM	331	244
CASH RECEIVED FROM HEALTH RESEARCH COLLABORATION	2,700	3,200
CASH PAID FOR GRANTS AND AWARDS	(36,061)	(31,099)
CASH PAID FOR PROGRAM OPERATION	(1,288)	(878)
CASH PAID FOR ADMINISTRATION	(2,746)	(2,274)
NET CASH (USED IN) GENERATED THROUGH OPERATING ACTIVITIES	(786)	2,232
INVESTING ACTIVITIES:		
CASH PAID FOR PURCHASE OF CAPITAL ASSETS	(126)	(453)
PROCEEDS ON DISPOSAL OF CAPITAL ASSETS	1	–
NET CASH USED IN INVESTING ACTIVITIES	(125)	(453)
FINANCING ACTIVITIES:		
CASH PAID FOR CAPITAL LEASE OBLIGATION REPAYMENTS	(61)	(82)
NET CASH USED IN FINANCING ACTIVITIES	(61)	(82)
NET INCREASE (DECREASE) IN CASH FOR THE YEAR	(972)	1,697
CASH AT BEGINNING OF YEAR	10,055	8,358
CASH AT END OF YEAR	$ 9,083	$ 10,055
CASH	$ 3,434	$ 3,843
RESTRICTED CASH	5,649	6,212
	$ 9,083	$ 10,055

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

March 31, 1999

NOTE 1 AUTHORITY AND PURPOSE

The Alberta Heritage Foundation for Medical Research (the Foundation) operates under the authority of the Alberta Heritage Foundation for Medical Research Act, Chapter A–26, Revised Statutes of Alberta 1980, as amended.

The Foundation supports and promotes research in Alberta to improve health and thereby the quality of life of Albertans and people throughout the world.

NOTE 2 SIGNIFICANT ACCOUNTING POLICIES AND REPORTING PRACTICES

(a) Basis of Presentation

These consolidated financial statements include the accounts of the Alberta Foundation for Health Research, which operates under The Alberta Companies Act and is a registered charitable organization for income tax purposes. The Alberta Foundation for Health Research activities are directed to the support and advancement of the Foundation.

(b) Capital Assets and Amortization

Capital assets are recorded at cost less accumulated amortization. Capital assets, except for leasehold improvements, are amortized on a straight–line basis over their estimated useful lives at the following annual rates:

Furniture	10%
Office equipment	20%
Computer equipment	33%
Computer equipment under capital lease	33%

Leasehold improvements are amortized on a straight-line basis over the term of the lease.

(c) Cash and Restricted Cash

Cash and restricted cash consist of deposits in the Consolidated Cash Investment Trust Fund of the Province of Alberta. The Fund is invested primarily in securities maturing in less than one year which are either issued or guaranteed by the Canadian federal and provincial governments, deposits given by or guaranteed by chartered banks, or short-term investment-grade-quality notes of Canadian corporations. Interest is earned on the daily cash balance at the average rate or earnings of the Fund which varies depending on prevailing market interest rates.

Restricted cash represents unspent contributions that are subject to externally imposed restrictions related to the Medical Innovation Program.

(d) Fair Value of Financial Instruments

Short–term instruments are valued at their carrying amounts included on the consolidated statements of financial position, which are reasonable estimates of fair value due to the relatively short period to maturity of the instruments. This approach applies to cash, restricted cash, accounts receivable, advances, accounts payable and accrued liabilities, accrued retirement allowance, deferred lease inducement and capital lease obligation.

(e) Revenue Recognition

Restricted contributions are recognized as revenue in the year in which the related expenses are incurred. Restricted contributions received for future expenses are deferred until that future period when they are transferred to revenue.

Unrestricted contributions are recognized as revenue in the current period if the amount to be received can be reasonably estimated and collection is reasonably assured. Endowment contributions are recognized as direct increases in net assets.

Restricted investment income is recognized as a revenue in the year in which the related expenses are incurred. Unrestricted investment income is recognized as revenue when earned.

Recoveries on technology commercialization projects are recognized when performance requirements are satisfied, the amount to be received can be reasonably estimated and collection is reasonably assured.

(f) Grants and Awards Expense

Grants and awards approved by the Trustees of the Foundation are recorded as expense when the awardee has been notified of the amount of the award and all terms and conditions of eligibility for payment of the award have been met.

(g) Pension

Pension Expense

Salaries and benefits include employer pension plan contributions made during the year, the amortization of experience gains and losses, and the increase in accrued retirement allowance.

Deferred Pension Costs

Deferred pension costs represent the cumulative difference between the amounts expensed and the funding contributions required under the Foundation's pension plan.

Accrued Retirement Allowance

Accrued retirement allowance consists of the unfunded liability of a retirement allowance for the Foundation's President.

NOTE 2 SIGNIFICANT ACCOUNTING POLICIES AND REPORTING PRACTICES (CONTINUED)

(h) Lease Inducement

The lease inducement, a cash payment received by the Foundation on the lease for office premises, has been deferred and is accounted for as a reduction of office rental expense on a straight–line basis over the term of the lease.

NOTE 3 ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH ENDOWMENT FUND

The Endowment Fund operates pursuant to the Alberta Heritage Foundation for Medical Research Act and consists of an initial endowment of $300,000,000 from the Alberta Heritage Savings Trust Fund together with cumulative earnings thereon, less cumulative transfers to the Foundation.

Transfers to the Foundation are available at the request of the Trustees of the Foundation provided that such transfers do not result in the net assets of the Endowment Fund, valued at cost, being less than the initial endowment.

At March 31, 1999 the net assets of the Endowment Fund valued at cost were approximately $887 million (1998 $805 million) and valued at market were approximately $973 million (1998 $975 million).

NOTE 4 CAPITAL ASSETS

(THOUSANDS OF DOLLARS)

	1999			1998
	COST	ACCUMULATED AMORTIZATION	NET BOOK VALUE	NET BOOK VALUE
FURNITURE AND EQUIPMENT	$ 342	$200	$ 142	$ 163
COMPUTER EQUIPMENT	784	424	360	90
COMPUTER EQUIPMENT UNDER CAPITAL LEASE	148	118	30	62
LEASEHOLD IMPROVEMENTS	122	69	53	68
ASSETS UNDER CONSTRUCTION	1	–	1	354
	$ 1,397	$ 811	$ 586	$ 737

NOTE 5 PENSION PLAN

The Foundation's pension plan is a defined benefit plan. Benefits are based on years of service and average salary in the final years of employment.

Pension expense includes the amortization of experience gains and losses. These amounts are being amortized on a straight–line basis over periods from 14 to 21 years. The cumulative difference between the amounts expensed and the funding contributions required is shown on the statement of financial position as deferred pension costs of $73,400 (1998 $36,600).

NOTE 5 PENSION PLAN (CONTINUED)

The Plan's status as at March 31, 1999 is as follows:

(THOUSANDS OF DOLLARS)

	1999	1998
ASSETS	$ 1514	$ 1359
LESS ACTUARIAL VALUE OF ACCRUED PENSION BENEFITS	1155	1022
EXCESS BALANCE	$ 359	$ 337

The value of accrued pension benefits was determined by an actuarial valuation as at March 31, 1998 extrapolated to March 31, 1999. The actuarial valuation was determined using the projected benefit method prorated on service. Assumptions used in the valuations are based on the Foundation's best estimate of future events. The Plan's future experience will inevitably vary, perhaps significantly, from the assumptions. Any differences between the actuarial assumptions and future experience will emerge as gains or losses in future valuations and will be amortized over the expected average remaining service life of the employee group.

Retirement Allowance

In December 1993, the Board of Trustees approved a retirement allowance package for the President. The unfunded liability at March 31, 1999 of $183,500 (1998 $133,500) has been accrued and expensed. This liability was determined by an actuary using the same assumptions that were used to value the pension plan.

NOTE 6 CAPITAL LEASE OBLIGATION

The capital lease on computer equipment bears an interest rate of 5.25% and matures on July 1, 1999. Future repayments which include a provision for a $25,170 buyout option are as follows:

YEAR ENDED MARCH 31, 2000	$ 55,401
TOTAL MINIMUM LEASE PAYMENTS	55,401
LESS IMPUTED INTEREST	(328)
	$ 55,073

The capital lease relates to approximately $297,000 of computer equipment. The Foundation has included $147,676 of this equipment in capital assets (Note 4). In 1997, the balance was expensed since the equipment was transferred to the regional health authorities and provincial boards as part of the SEARCH program.

NOTE 7 DEFERRED CONTRIBUTIONS

Deferred contributions represent unspent resources externally restricted under the Medical Innovation Program and the Health Research Collaboration Agreement. Amounts are amortized to revenue to the extent of expenses incurred under these programs during the current period. Changes in the deferred contributions balance are as follows:

	1999	1998
(THOUSANDS OF DOLLARS)		
CONTRIBUTIONS RECEIVED DURING THE YEAR:		
TRANSFERS FROM ALBERTA HEALTH UNDER THE HEALTH RESEARCH COLLABORATION AGREEMENT	$ 2,700	$ 3,200
INTEREST	303	244
RECOVERIES ON TECHNOLOGY COMMERCIALIZATION	28	–
	3,031	3,444
LESS AMOUNTS RECOGNIZED AS REVENUE IN THE CURRENT YEAR:		
HEALTH RESEARCH COLLABORATION	3,153	2,980
MEDICAL INNOVATION PROGRAM	2,134	1,203
	5,287	4,183
DECREASE DURING THE YEAR	(2,256)	(739)
BALANCE AT BEGINNING OF YEAR	8,204	8,943
BALANCE AT END OF YEAR	$ 5,948	$ 8,204
THE BALANCE IS COMPRISED AS FOLLOWS:		
MEDICAL INNOVATION PROGRAM	3,549	5,351
HEALTH RESEARCH COLLABORATION	2,399	2,853
	$ 5,948	$ 8,204

NOTE 8 NET ASSETS

Operations include the biomedical and health programs of the Foundation which are funded from the transfers from the Endowment Fund and available cash balances. The Foundation's policy is to retain funds in the Endowment Fund and transfers are made only on an as needed basis.

NOTE 9 OTHER PROGRAMS

(a) Alberta Foundation for Health Research

The Alberta Foundation for Health Research, a wholly owned subsidiary of the Foundation, operates under The Alberta Companies Act and is a registered charity for income tax purposes. The Foundation's activities are directed to promote and support medical and health research.

(b) Medical Innovation Program

The Foundation administers funds for the Medical Innovation Program on behalf of the Minister of Economic Development. The Program funds the early stages for commercial development of medical and health related technologies.

(c) Health Research Collaboration

The Foundation and Alberta Health have entered into an agreement to facilitate and enhance health research and health technology assessment and their dissemination in the Province of Alberta.

NOTE 10 RECOVERIES ON TECHNOLOGY COMMERCIALIZATION

The Foundation has entered into various agreements to fund technology commercialization projects. The projects involved have high scientific merit, but are speculative with both technical and commercial risk. Any recoveries by the Foundation under these agreements will be long term, in some cases at least ten years. In addition to recoveries, some agreements contain a provision for future royalty payments. Amounts ultimately receivable by the Foundation are not determinable at this time and will be recognized as revenue when they are due and collection is reasonably assured.

NOTE 11 SALARIES AND BENEFITS

	1999			1998		
	SALARIES(1)	BENEFITS(2)	TOTAL(3)	SALARIES(1)	BENEFITS(2)	TOTAL(3)
CHAIRMAN	$ 12,281	$ –	$ 12,281	$ 10,405	$ –	$ 10,405
BOARD OF TRUSTEES	78,588	1,098	79,686	73,940	1,007	74,947
PRESIDENT AND CHIEF EXECUTIVE OFFICER	188,333	30,705(4)	219,038	178,000	28,345	206,343
	$ 279,202	$ 31,803	$ 311,005	$ 262,345	$ 29,352	$ 291,695

(1) Salaries include regular base pay, overtime, retainers, honoraria, and any other direct cash renumeration.

(2) Benefits include the Foundation's share of all employee benefits and contributions or payments made on behalf of employees including vacation payouts, pension, health care, dental coverage, out–of–country medical benefits, medical benefits, group life insurance, accidental disability and dismemberment insurance, long and short–term disability plans and professional memberships.

(3) Salaries and benefits are distributed to various expense categories including committee meetings and fees, salaries and benefits and office administration.

(4) Contributions for accrued retirement allowance were $17,400 in 1999 ($10,000 1998).

NOTE 12 COMMITMENTS

(a) Office Premises

The Foundation has entered into a 65 month lease for office premises.

This lease expires on May 31, 2001.

(b) Total commitments pertain to the following fiscal years:

	GRANTS AND AWARDS	OFFICE PREMISES	TOTAL
(THOUSAND OF DOLLARS)			
1999–2000	$ 26,248	$ 48	$ 26,296
2000–2001	13,146	57	13,203
2001–2002	8,273	10	8,283
2002–2003	5,464	–	5,464
2003–2004	2,645	–	2,645
	$ 55,776	$ 115	$ 55,891

NOTE 13 BUDGET

The budget process involves the determination of the cost for the estimated number of investigators sponsored for Foundation awards and meeting standards of excellence which the Foundation could support within the spending guidelines and program objectives laid out by the Board of Trustees of the Foundation. Variance from budget is determined in a large part by the number and quality of actual applications received and deferred or declined awards.

The 1998–99 budget was approved by the Board of Trustees in March 1998. Following is the consolidated budget:

	ACTUAL	BUDGET
(THOUSAND OF DOLLARS)		
REVENUE	$ 41,565	$ 40,745
GRANTS AND AWARDS	(36,922)	(38,415)
PROGRAM OPERATION	(1,288)	(1,934)
ADMINISTRATION	(3,019)	(2,827)
EXCESS (DEFICIENCY) OF REVENUE OVER EXPENSE	$ 336	$ (2,431)

Funds are budgeted and transferred from the Endowment Fund on an as needed basis.

NOTE 14 UNCERTAINTY DUE TO THE YEAR 2000

The year 2000 issue is the result of some computer systems using two digits rather than four to define the applicable year. Government computer systems that have date sensitive software may recognize a date using "00" as the year 1900 rather than the year 2000, which could result in miscalculations or system failures. In addition, similar problems may arise in some systems if certain dates in 1999 are not recognized as a valid date or are recognized to represent something other than a date. The effects of the year 2000 issue may be experienced before, on, or after January 1, 2000. If not addressed, the effect on operations and financial reporting may range from minor errors to significant systems failure that could affect the ability to conduct some government operations. Despite the government's efforts to address this issue, it is not possible to be certain that all aspects of the year 2000 issue affecting the government, including those related to the efforts of customers, suppliers and other third parties, will be fully resolved.

NOTE 15 APPROVAL OF FINANCIAL STATEMENTS

These financial statements were reviewed by the Audit Committee and recommended to the Board of Trustees for approval.

Alberta Foundation for Health Research

FINANCIAL STATEMENTS

March 31, 1999

AUDITOR'S REPORT 108

STATEMENT OF FINANCIAL POSITION 109

STATEMENT OF REVENUE AND EXPENSE 109

STATEMENT OF CHANGES IN NET ASSETS 110

STATEMENT OF CASH FLOWS 110

NOTES TO THE FINANCIAL STATEMENTS 111

AUDITOR’S REPORT

To the Trustees of the Alberta Foundation for Health Research

I have audited the statement of financial position of the Alberta Foundation for Health Research as at March 31, 1999 and the statements of revenue and expense, changes in net assets, and cash flows for the year then ended. These financial statements are the responsibility of the Foundation’s management. My responsibility is to express an opinion on these financial statements based on my audit.

I conducted my audit in accordance with generally accepted auditing standards. Those standards require that I plan and perform an audit to obtain reasonable assurance whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation.

In my opinion, these financial statements present fairly, in all material respects, the financial position of the Foundation as at March 31, 1999 and the results of its operations and the changes in its financial position for the year then ended in accordance with generally accepted accounting principles.

Peter Valentine
FCA
Auditor General

Edmonton, Alberta
June 25, 1999

Alberta Foundation for Health Research

STATEMENT OF FINANCIAL POSITION

for the year ended March 31, 1999

	1999	1998
ASSETS		
CASH	$134,312	$610,582
LIABILITIES AND NET ASSETS		
NET ASSETS	$134,312	$610,582

The accompanying notes are part of these financial statements.

Alberta Foundation for Health Research

STATEMENT OF REVENUE AND EXPENSE

for the year ended March 31, 1999

	1999	1998
REVENUE		
DONATIONS	$ –	$ 602,329
INTEREST	31,035	11,395
	31,035	613,724
EXPENSES		
GRANTS	500,000	–
NEWSLETTER	2,308	–
PROFESSIONAL FEES	4,997	3,437
	507,305	3,437
EXCESS (DEFICIENCY) OF REVENUE OVER EXPENSE FOR THE YEAR	$ (476,270)	$ 610,287

Alberta Foundation for Health Research

STATEMENT OF CHANGES IN NET ASSETS

for the year ended March 31, 1999

	UNRESTRICTED	1999	1998
BALANCE AT BEGINNING OF YEAR	$ 610,582	$ 610,582	$ 295
EXCESS (DEFICIENCY) OF REVENUE OVER EXPENSE	(476,270)	(476,270)	610,287
BALANCE AT END OF YEAR	$ 134,312	$ 134,312	$ 610,582

Alberta Foundation for Health Research

STATEMENT OF CASH FLOWS

for the year ended March 31, 1999

	1999	1998
OPERATING ACTIVITIES:		
CASH RECEIVED FROM OPERATIONS	$ 31,035	$ 613,743
CASH PAID FOR PROGRAM OPERATIONS	(507,305)	(3,437)
NET INCREASE (DECREASE) IN CASH FOR THE YEAR	(476,270)	610,306
CASH AT BEGINNING OF YEAR	610,582	276
CASH AT END OF YEAR	$ 134,312	$ 610,582

NOTES TO THE FINANCIAL STATEMENTS

March 31, 1999

NOTE 1 AUTHORITY AND PURPOSE

The Alberta Foundation for Health Research, a subsidiary of the Alberta Heritage Foundation for Medical Research, operates under The Alberta Companies Act and is a registered charity for income tax purposes. The Foundation was incorporated on November 17, 1994 and commenced operations during 1998. The Foundation's activities are directed to promote and support medical and health research.

NOTE 2 SIGNIFICANT ACCOUNTING POLICIES AND REPORTING PRACTICES

(a) Cash

Cash consists of deposits in the Consolidated Cash Investment Trust Fund of the Province of Alberta. The Fund is invested primarily in securities maturing in less than one year which are either issued or guaranteed by the Canadian federal and provincial governments, deposits given by or guaranteed by chartered banks, or short-term investment-grade-quality notes of Canadian corporations. Interest is earned on the daily cash balance at the average rate or earnings of the Fund which varies depending on prevailing market interest rates.

(b) Fair Value of Financial Instruments

Short-term instruments are valued at their carrying amounts included on the consolidated statements of financial position, which are reasonable estimates of fair value due to the relatively short period to maturity of the instruments. This approach applies to cash and accounts receivable.

(c) Revenue Recognition

Restricted contributions are recognized as revenue in the year in which the related expenses are incurred. Restricted contributions received for future expenses are deferred until that future period when they are transferred to revenue.

Unrestricted contributions are recognized as revenue in the current period if the amount to be received can be reasonably estimated and collection is reasonably assured. Endowment contributions are recognized as direct increases in net assets.

Restricted investment income is recognized as revenue in the year in which the related expenses are incurred. Unrestricted investment income is recognized as revenue when earned.

NOTE 3 **BUDGET**

As the Foundation commenced operations in 1998 and has had limited activity, a budget was not prepared for 1998-99. In future, the Board will determine an appropriate budgeting process, given that donations are unpredictable and operating expenses are minimal.

NOTE 4 **UNCERTAINTY DUE TO THE YEAR 2000**

The year 2000 issue is the result of some computer systems using two digits rather than four to define the applicable year. Government computer systems that have date sensitive software may recognize a date using "00" as the year 1900 rather than the year 2000, which could result in miscalculations or system failures. In addition, similar problems may arise in some systems if certain dates in 1999 are not recognized as a valid date or are recognized to represent something other than a date. The effects of the year 2000 issue may be experienced before, on, or after January 1, 2000. If not addressed, the effect on operations and financial reporting may range from minor errors to significant systems failure that could affect the ability to conduct some government operations. Despite the government's efforts to address this issue, it is not possible to be certain that all aspects of the year 2000 issue affecting the government, including those related to the efforts of customers, suppliers and other third parties, will be fully resolved.

NOTE 5 **APPROVAL OF FINANCIAL STATEMENTS**

These financial statements were reviewed and approved by the Board of Directors.

The series, *Essence of Life*, by Koichi Yamamoto

Credits

Editor: Kathleen Thurber

Writers: Rhonda Lothammer, Darren Nichols, Kathleen Thurber

Copy Editor: Natalie King

Designer: Interpret Design Inc.

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